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14. ABSTRACT The long-term goal of this research is to advance orthopedic surgery by designing implantable, miniature, passive mechanisms, such as artificial insertable rods and tendon networks, for enhancing the functional attachment of muscle to tendon(s) and bone and creating superior and customizable movement and force transmission. The specific object goal of this work is to design, fabricate, and validate a biocompatible implantable mechanism that enables the surgical construction of a "differential mechanism" using existing biological tendons in order to improve the routing of forces and movements between muscle and tendons in the tendon-transfer surgery for high median-ulnar nerve trauma. The key findings in this period relating to the project goals are as follows: 1) The mechanical effect of the implant on the muscle-tendon biomechanics has been validated. 2) Progress in implant design and fabrication is excellent. 3) Preliminary development and validation of non-fouling coatings for the implant has been completed.					
15. SUBJECT TERMS Orthopedic surgery, biomechanics, biomaterials, implant design, non-fouling coating, robotics, cadaver, live-animal trials.					
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1. INTRODUCTION: *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

The subject of this research is to advance orthopedic surgery by designing implantable, miniature, passive mechanisms, such as artificial insertable rods and tendon networks, for enhancing the functional attachment of muscle to tendon(s) and bone. When used in place of the current surgical practice of direct suture repair to attach muscle to tendon(s) and bone, the implantable mechanisms will enable superior and customizable force and movement transmission using the patient's natural musculature without external power or control input. This work will design these implants so that the mechanism may be surgically constructed *in situ* by using the existing biological tendons maximally. The purpose of this research is to design, fabricate, and validate a biocompatible implantable mechanism that enables the surgical construction of a "differential mechanism" using existing biological tendons in order to improve the routing of forces and movements between muscle and tendons in the tendon-transfer surgery for high median-ulnar nerve trauma. The scope of the research is to 1) design and fabricate the implant using biocompatible materials, 2) develop a non-fouling coating for the implant, 3) validate the implant biomechanical function and coating using biomechanical simulations, human cadaver experiments, and live-animal experiments.

2. KEYWORDS: *Provide a brief list of keywords (limit to 20 words).*

Orthopedic surgery, biomechanics, biomaterials, implant design, non-fouling coating, robotics, cadaver, live-animal trials.

3. ACCOMPLISHMENTS: *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.*

What were the major goals of the project?

List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project identify these dates and show actual completion dates or the percentage of completion.

1. The primary goal of this project is to develop implantable passive mechanisms for orthopedic surgery.
2. Here are the subtasks that were identified in the approved SOW for year 1:
 - Subtask 1.1A: Identify bioinert material for implant components (months 1-2)
 - Subtask 1.1B: Identify the post-surgical musculoskeletal function desired and develop metrics for evaluating the implants (months 1-2)
 - Subtask 1.1C: Identify implant dimensions for use in human forearm (months 1-4)
 - Subtask 1.1D: Identify mechanical stresses expected in the implant during use (months 1-4)
 - Subtask 1.1E: Design implant in CAD program (months 1-5)
 - Subtask 1.1F: Fabricate implant (months 5-6)
 - Subtask 1.1G: Conduct fatigue and stability analysis (months 7-8)

- Subtask 1.1H: Conduct pilot tests on implant using robotic platform (months 8-9)
- Subtask 1.1I: Revise design and fabricate as needed (months 10-11)
- Subtask 1.1J: Conduct pilot cadaver tests on implant (months 11-12)
- Subtask 1.3A: Build relevant upper-extremity biomechanical models in OpenSim (month 1)
- Subtask 1.3B: Incorporate implants into OpenSim models (month 2)
- Subtask 1.3C: Develop simulations of finger movements in free space and grasping tasks (months 1-3)
- Subtask 1.3D: Identify the relationship between implant parameters and hand function enable (months 2-4)
- Subtask 1.3F: Provide input to Task T1.1 (months 5-10, 13-14)
- Subtask 1.3G: Design cadaver experiment set-up (months 3-4)
- Subtask 1.3H: Procure components for set-up (month 5)
- Subtask 1.3I: Construct set-up (month 6)
- Subtask 1.3J: Test set-up on passive robotic fingers at OSU (months 7-8)
- Subtask 1.3K: Revise set-up design and repeat test as needed (month 9)
- Subtask 1.3L: Procure first set of cadavers (months 10)
- Subtask 1.3M: Conduct pilot studies on cadavers to inform the design process (months 11-12)
- Subtask 2.1A: Surface activation of Kevlar with hydroxyethyl methacrylate RF-plasma (months 1-4)
- Subtask 2.1B: Surface activation of PVDF with hydroxyethyl methacrylate RF-plasma (months 2-5)
- Subtask 2.1C: Surface activation of UHMWPE with hydroxyethyl methacrylate RF-plasma (months 3-6)
- Subtask 2.1D: Derivatization of the -OH surfaces with a RAFT or ATRP initiator (months 2-4)
- Subtask 2.1E: Growth of a brush of sulfobetaine methacrylate polymer onto the surface (months 3-6)
- Subtask 2.1F: Surface analysis to confirm good coating quality (months 7-10)
- Subtask 2.1G: Stability studies in vitro to ensure that coating delamination does not occur (months 7-10)
- Subtask 2.1H: Assessment of wear of the coating under mild abrasion (months 10-12)

What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

In reference to the tasks listed for annual report, the following were achieved:

- Subtask 1.1A: Identify bioinert material for implant components
 - Polypropylene, Ultra High Molecular Weight Polyethylene, and Polyurethane will be used initially as the biocompatible material for the implants. All three materials are suitable. Each have their advantages, including aspects such as strength, manufacturability, and suitability for coating application.
- Subtask 1.1B: Identify the post-surgical musculoskeletal function desired and develop metrics for evaluating the implants
 - Metrics such as the differential action between the fingers during grasping (how much one finger can flex when another finger has stopped after making contact with the object to be grasped) was identified as a key metric for implant performance. Other factors are the maximum force applied by the fingers, the distribution of forces between the fingers, and maximizing the differential action for a fixed excursion of the actuating muscle tendon.
 - In order to get the appropriate weights for each factor, a Delphi panel was also conducted at the Hand Wrist Biomechanics International 2017 symposium across hand surgeons and hand therapists. We received excellent feedback on what surgeons believe are important aspect in grasping task, what is useful for evaluating and treating patients before and after surgery for High Median Ulnar Palsy, and what metrics of implantable mechanism are most pivotal to their success. As part of the Delphi panel process, we have sent out the second survey using the information gained from the first survey. The survey is available in the appendix. The results from the first survey are as follows:
 - Surgeons prefer power grasps over precision grasps for high median-ulnar palsy patients post-surgery.
 - The finger-tip force of the middle finger and index finger should be equal, while the ring and little fingers should have 63% of index force.
 - Within precision grasps, the thumb-index and thumb-index-middle precision grasps are most important for daily activities.
 - The most important feature of a power grasp is its hold duration.
 - Mobile phones are the most commonly used item for people with high median-ulnar palsy
 - The most applicable animal model for studying the tendon-transfer surgery for high median-ulnar palsy is the monkey (ranks at 4.33 out of a maximum of 5), while the chicken is at 3.17 out of 5.

- Checking for tenodesis and finger range of motion are useful methods for predicting finger movement and hand flexion post-surgery for high median ulnar palsy
 - Hand function before and after tendon-transfer surgery is evaluated using grip and pinch strength, and assessment of finger position, motion, and strength.
 - A balanced distribution of fingertip forces is the most important factor in designing a passive mechanical implant. Other factors include smaller muscle force to make contact with an object and little resistance force (biologically or mechanically)
 - “Blinded” methods that a surgeon or rehab expert can use to evaluate finger movement following post-surgery include making a composite fist, grip and pinch strength, and writing one's signature
 - The most important factor in designing the implant is reduced injury to surrounding tissue. Other important factors include ability to salvage in case of failure and the action of antagonist muscle is unaffected.
 - Post-surgery healing is monitored through range of motion, strength and physical examinations.
 - Finger motion, stiffness, lack of sensation and range of motion are important when gauging whether another surgery is needed
 - Non-invasive methods for checking the amount of scar tissue that has been developed are ultrasound, MRI, tenodesis, or range of motion
 - Three-finger grasps are slightly more important (0.53 with 0.5 being equal) that two fingers when grasping an object.
- Subtask 1.1C: Identify implant dimensions for use in human forearm
 - This task is complete. The two critical dimensions of the implant candidates for the human forearm are the width (W) and height (H) of a triangle formed by bifurcated tendon and inserted implant, as shown in Fig.1.1C. For the human forearm, the width W was chosen to be 1.5 cm and the height H 0.2 cm.

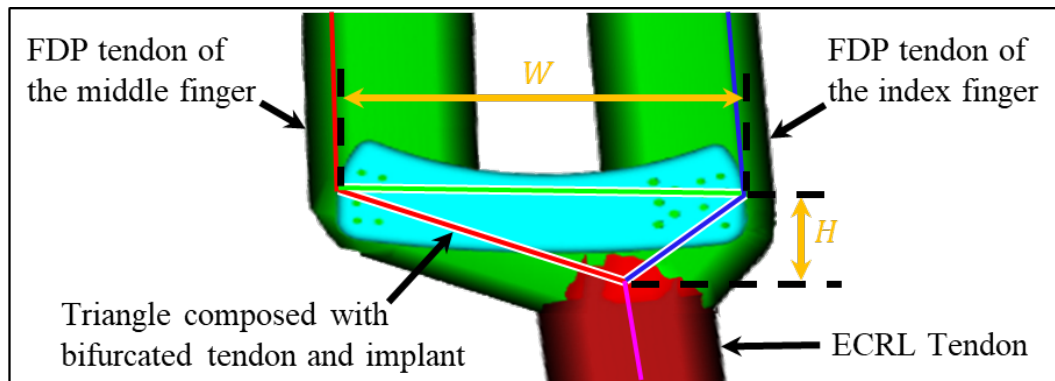


Fig.1.1C. Triangle formed by tendon and implant (lines with white outline).

- Subtask 1.1D: Identify mechanical stresses expected in the implant during use
 - A mechanics (quasistatic) analysis was conducted to identify the forces on different versions of the implant during operation. This was conducted using mathematical mechanics models and computational models in SolidWorks. See figures below for one example.
 - SolidWorks simulations were produced for both chicken and human sized tendons.

- In these simulations, the tendons are loaded axially with 100 N on the single end, and fixed on the opposite two ends.

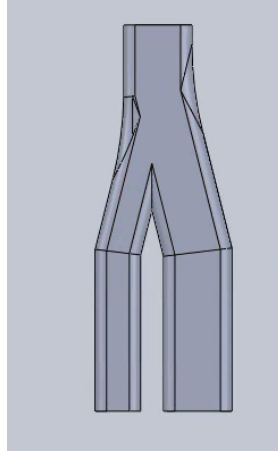


Fig.1.1D-1. Chicken tendon model

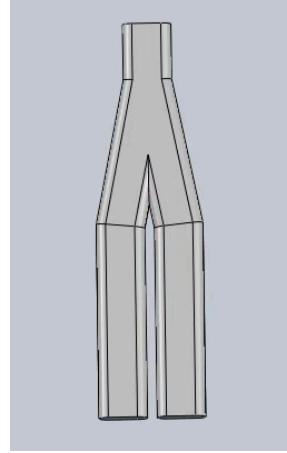


Fig.1.1D-2. Human tendon model

- In the chicken model, placing the implant between the tendons increased the maximum stress 57.22 MPa (Fig.1.1D-3). The additional muscle load of 100N increased stress further. The U-shaped implant created a maximum stress concentration of 219.7 MPa (283% increase), while the strut implant resulted in a maximum stress of 324.3 MPa (466.7% increase), as shown in Fig.1.1D-4 and 5. The increase in stress is expected. The implant is pushing the tendon apart creating stress concentrations on the interface between the tendon and the implant. The U-shaped implant provides more surface contact, and thus minimizes the maximum stress concentration. The implant will be made of a polyurethane (RPU 70). The flexural modulus of RPU 70 is 1.8 ± 0.3 GPa., making the implant sufficiently strong.

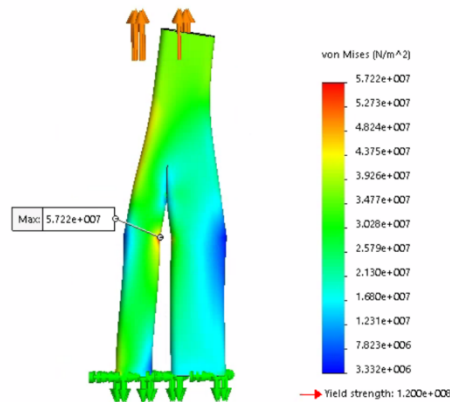


Fig.1.1D-3. Stress in chicken tendon without implant

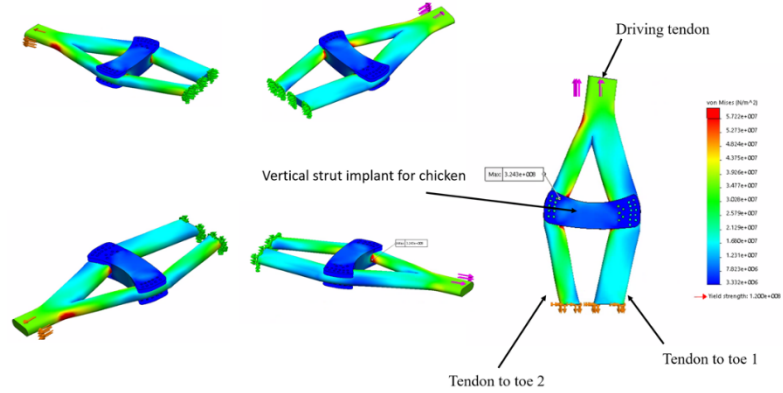


Fig.1.1D-4. Stress in chicken tendon with strut implant

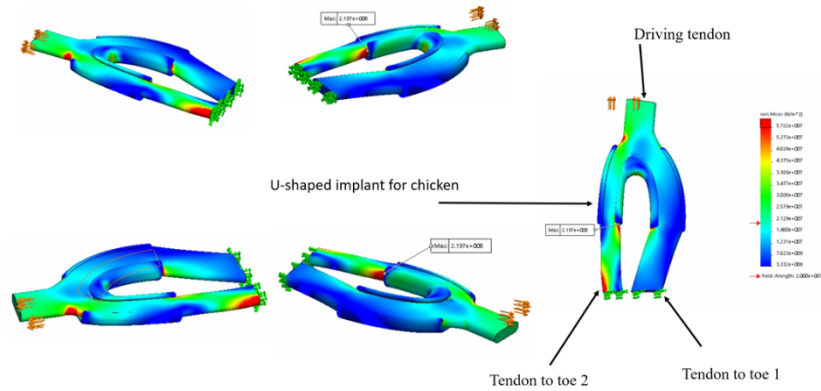


Fig.1.1D-5. Stress in chicken tendon with U-shaped implant

- Human case showed similar results to the chicken implants, as shown in Fig.1.1D-6 and 7. The stress concentrations appear in the expected locations. The initial maximum stress in the tendon without the implant is 36.24 MPa. The maximum stress concentration with the implant is 79.31 MPa (118% increase).

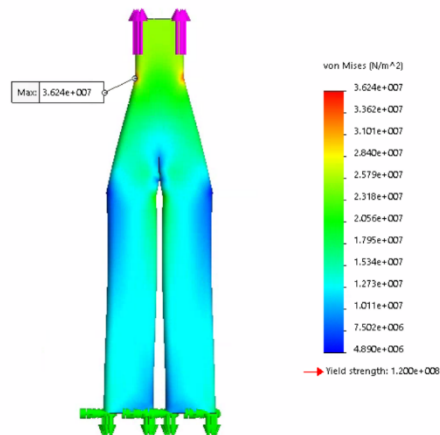


Fig.1.1D-6. Stress in human tendon without implant

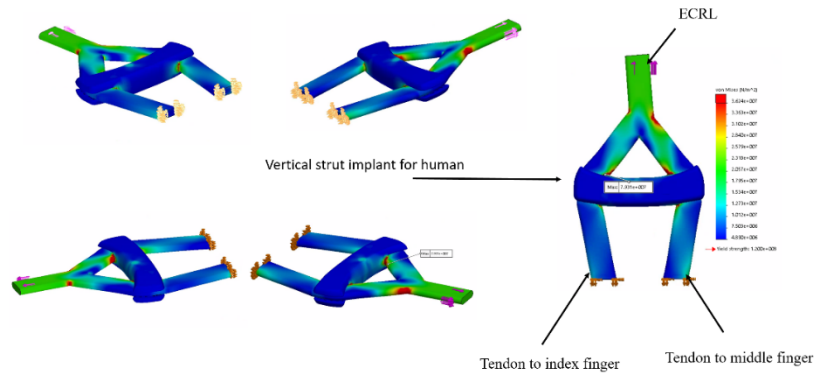


Fig.1.1D-7. Stress in human tendon with strut implant

- Subtask 1.1E: Design implant in CAD program
 - Currently, there are three implant designs: the strut (Fig.1.1E-1) and U-shaped implant (Fig.1.1E-2 and 3). Key features of the implants are as follows:
 - All the implants have grooves where the tendon will sit.
 - All implants have spikes to enable attachment to the tendon.
 - The spikes are directed inward to securely hold the tendon.
 - Both strut and U-shaped implant for chicken have channels for tissue glue inside the grooves to provide initial attachment between tendon and implant. Tissue glue will degrade over time, while scar tissue formation is expected to encapsulate the spikes to keep the tendon and implant attached firmly.

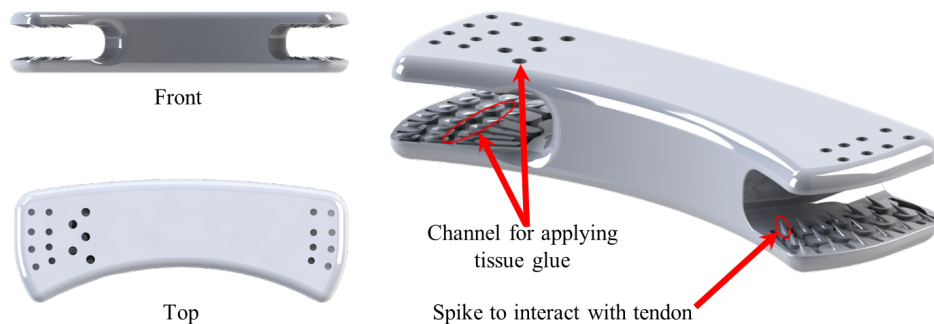


Fig.1.1E-1. Solidworks model of strut implant for both human and chicken. Note that the implant will be scaled up to fit a human from chicken version.

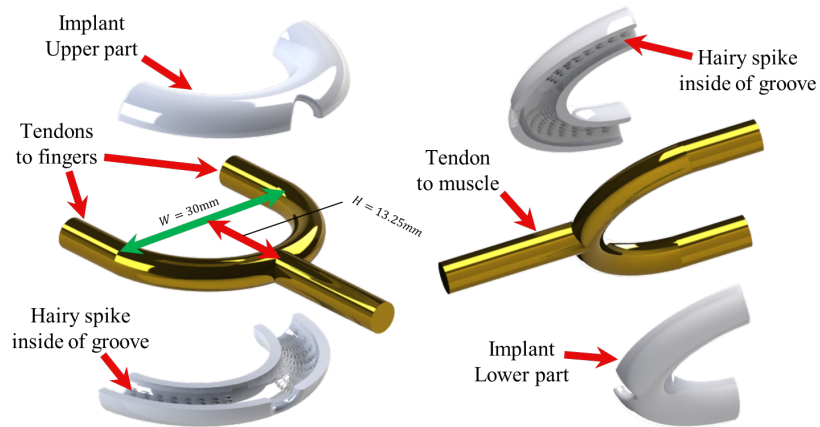


Fig.1.1E-2. Solidworks model of U-shaped implant for human.

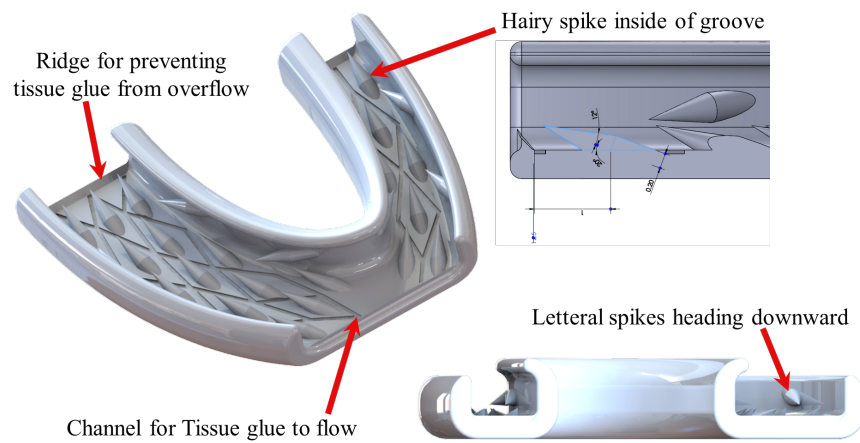


Fig.1.1E-3. Solidworks model of U-shaped implant for chicken.

- Subtask 1.1F: Fabricate implant (Won – take implant picture)
 - The implant designs have been 3D printed through a third-party vendor Carbon/Primary Manufacturing. They are fabricated with rigid polyurethane at a resolution of 70 microns.

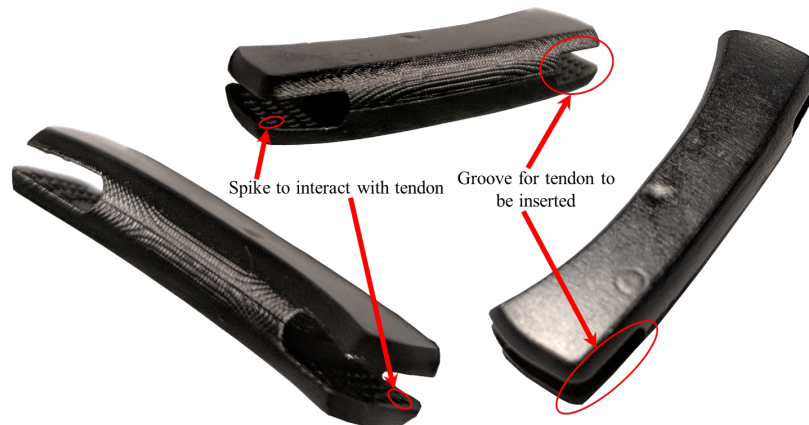


Fig.1.1F-1. Fabricated strut implant for both human and chicken.

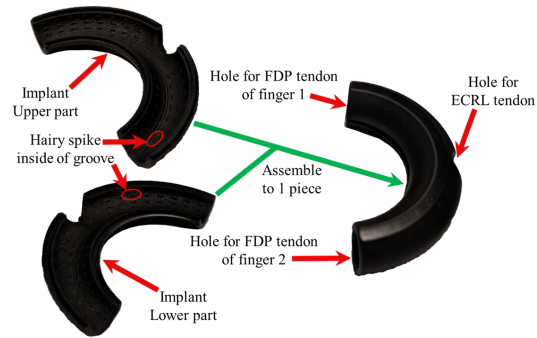


Fig.1.1F-2. Fabricated U-shaped implant for human.

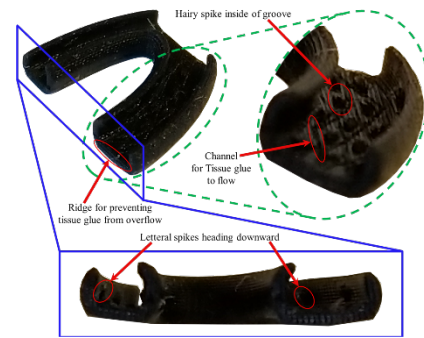


Fig.1.1F-3. Fabricated U-shaped implant for chicken.

- The implants have already been validated in a robotic testbed and in animal cadaver experiments. See Subtask 1.3J.
- Subtask 1.1G: Conduct fatigue and stability analysis
 - A stress analysis was conducted on the implant (see pic under subtask 1.1E) and a testbed has been constructed to validate the implant in fatigue testing (see pic below). The implant seen below was ran for 50,000 cycles with parameter of 12.5 mm excursion with an average force of 15 N.

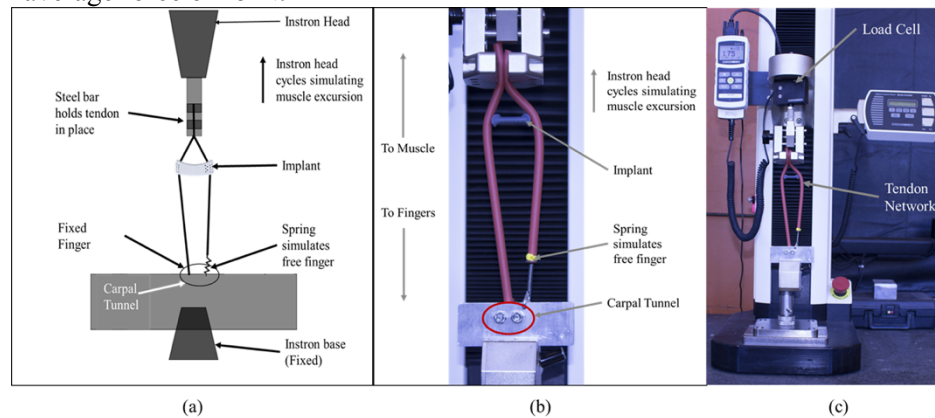


Fig. 1.1F Cycle testing apparatus (a) Mock sketch (b) tendon network (c) Testing Rig

- Subtask 1.1H: Conduct pilot tests on implant using robotic platform
 - A testing protocol known as "differential perturbation" was implemented to ascertain the performance of the implant. and 1.1H-3 illustrate the setup. One closed-loop-controlled DC motor (not pictured) acting as a muscle pulls on a para-aramid cable acting as a tendon. This tendon is connected to the MCP flexor tendons using either a suture (similar to how tendon-transfer surgeries work today) or using the implant (see Figure 1.1H-1). The index and middle fingers then rest on a differential perturbator which rotates to simulate uneven grip surfaces that the fingers might encounter (see Figure 1.1H-3). The finalized design of the perturbator is instrumented with loss-of-contact sensors and as well as a low-noise force-sensing load cell. The perturbator is mounted on an AdeptSix 300 industrial robot that rotates the perturbator about its axis. This setup allows us to quickly and accurately test a very large number of perturbation angles for various force-levels at the tendon prior to bifurcation.
 - An experiment was successfully conducted using a robotic platform (Utah/M.I.T. dexterous hand [1]) to show that the implant-based procedure provides better adaptation to the fingers during grasping when compared with using a suture-based procedure (See Fig 1.1H-1).
 - Specifically, it was shown that the implant enabled a robot's fingers to maintain equal contact with an object and apply equal forces (measured using load cells) even if the object changed orientation significantly after grasping. The study protocol featured angles of rotation of $\pm 30^\circ$ (in both the positive and negative directions of rotation about the mean position). Additionally, we swept through various force levels (3 to 30 Newtons) at the extrinsic flexor muscle applied to the para-aramid tendons. The trials were conducted 10 times for each angle-force combination for statistical significance. The fig 1.1H-2 shows the first set of results based on 1440 experimental trials; yellow represents maintaining contact; purple represents losing contact. Upon repeating the experiment using a revised differential perturbator with new loss-of-contact sensors and low-noise force-sensing load-cells yielded similar results (See Fig 1.1H-7). Additional analysis of the data collected from the load cells reveal that the forces applied by each finger at the endpoint is nearly equal across fingers, only showing small variations when comparing force changes relative to perturbation angle as is evident when comparing heatmaps in the two panels of Figures 1.1H-7. This demonstrates the ability of the implant to automatically, passively and evenly distribute forces across the fingers in the robotic hand. Clearly, the implant seems to act as a virtual gearing mechanism.
 - In contrast, the suture-based procedure failed to create equal forces across all the trials (See Fig 1.1H-4). Specifically, when the two bifurcated tendons to the index finger (digit 1) and middle finger (digit 2) are coupled to the MCP flexor by a simple suture, we see that there is a large set of angles for which we have a loss of contact (zero force). Also, it is clear that when one finger is making contact, the other digit has trouble doing the same, even at low angles as illustrated by the data in Figure 1.1H-5. This is best viewed when we look only at loss of contact, with the large black regions depicting major loss of contact of the digits from their supports. Indeed, the larger the object rotation, the better the adaptation provided by the implant when compared with the suture-based procedure.
 - In both cases (implant- and suture-based bifurcations), the variations in the endpoint-force heatmaps and the loss-of-contact plots between the two fingers may be attributed to the variations in the tendon lengths that arise from the suturing and knotting procedure of the tendons. The variation is minimal in the case of implant-based bifurcations simply because the virtual gearing of the implant automatically corrects for these variations

while the suture is simply unable to cope resulting in significant variation when a suture-based bifurcation is implemented.

- This work when combined with previous work [2, 3] that showed that the implant enables the fingers to adapt to external object shape even when actuation is position-controlled (rather than force-controlled) shows that the implant improves adaptive hand function under all physical-interaction scenarios. Overall, the suture-based approaches make it challenging for people with such tendon transfer surgeries will have trouble manipulating or even holding objects with any irregular surfaces, and the implant-based procedure helps overcome these challenges.

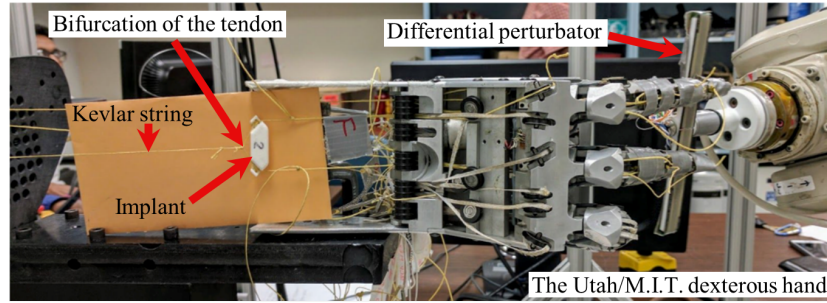


Fig.1.1H-1. Experimental set-up for the implant using robotic platform

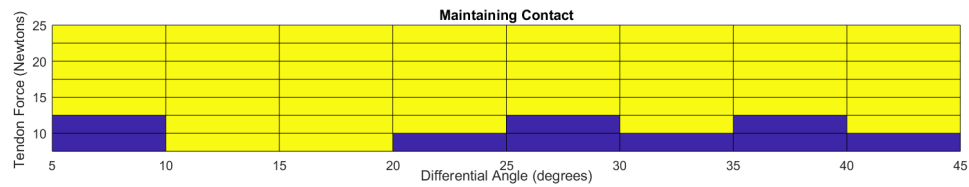


Fig.1.1H-2. The maintenance of contact of either finger using the implant for various values of tendon forces and differential angles including the implant on the tendon bifurcation. (Yellow section: contact maintained, Blue section: loss of contact)

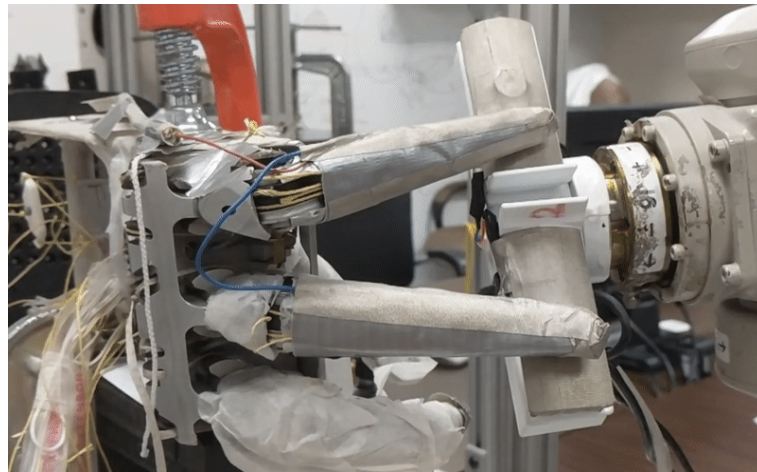


Fig.1.1H-3. The Utah/M.I.T. dexterous hand and differential perturbator.

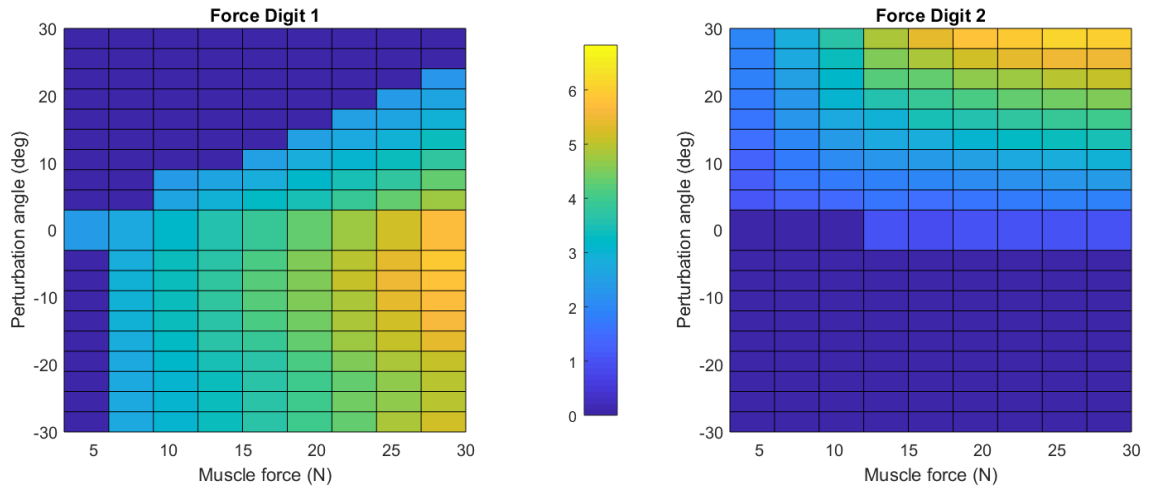


Fig.1.1H-4. The heatmaps shows digit force as recorded at the end of each digit for different tendon forces (from 0 to 30 Newtons) and perturbation angle (from 0 to ± 30 degrees) when the MCP flexors of the digits are coupled using a suture. The panel on the left is for the index finger (digit 1) while the panel on the right is for the middle finger (digit 2). Notice the large blue sections where contact is lost and force drops to zero.

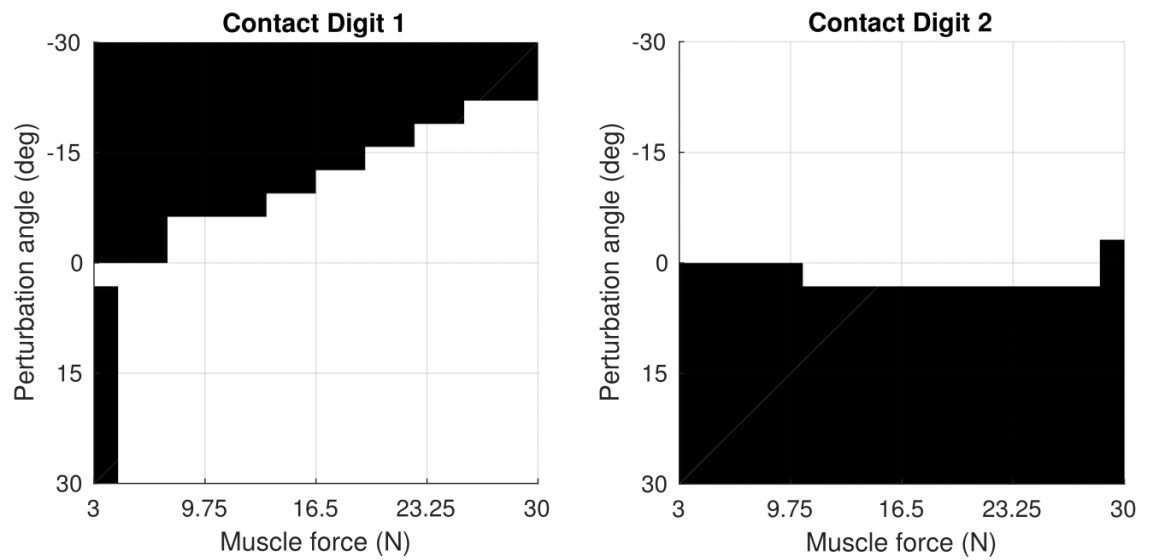


Fig.1.1H-5. The figure depicts loss of contact for each digit for 0 to 30 Newtons tendon forces at perturbation angles from 0 ± 30 degrees when they are coupled using a suture. The panel on the left is for the index finger (digit 1) while the panel on the right is for the middle finger (digit 2). The large black sections denote a loss of contact while the white sections denote the maintenance of contact.

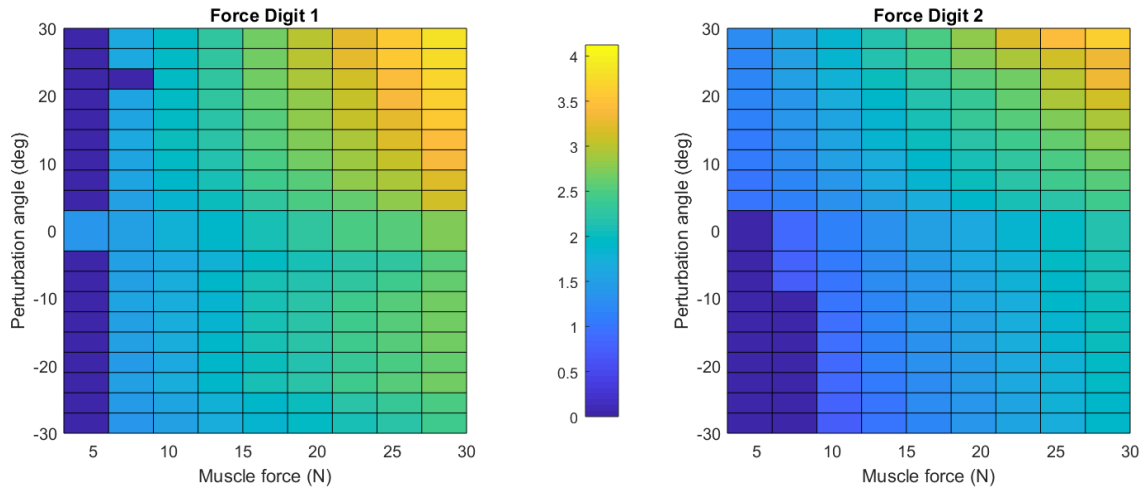


Fig.1.1H-6. The heatmaps shows digit force as recorded at the end of each digit for different tendon forces (from 0 to 30 Newtons) and perturbation angle (from 0 to ± 30 degrees) when the MCP flexors of the digits are coupled using the implant. The panel on the left is for the index finger (digit 1) while the panel on the right is for the middle finger (digit 2). There are much fewer sections when the force drops to zero. The force is also evenly distributed across both fingers, each of which produce very similar forces at every angle and tendon force level.

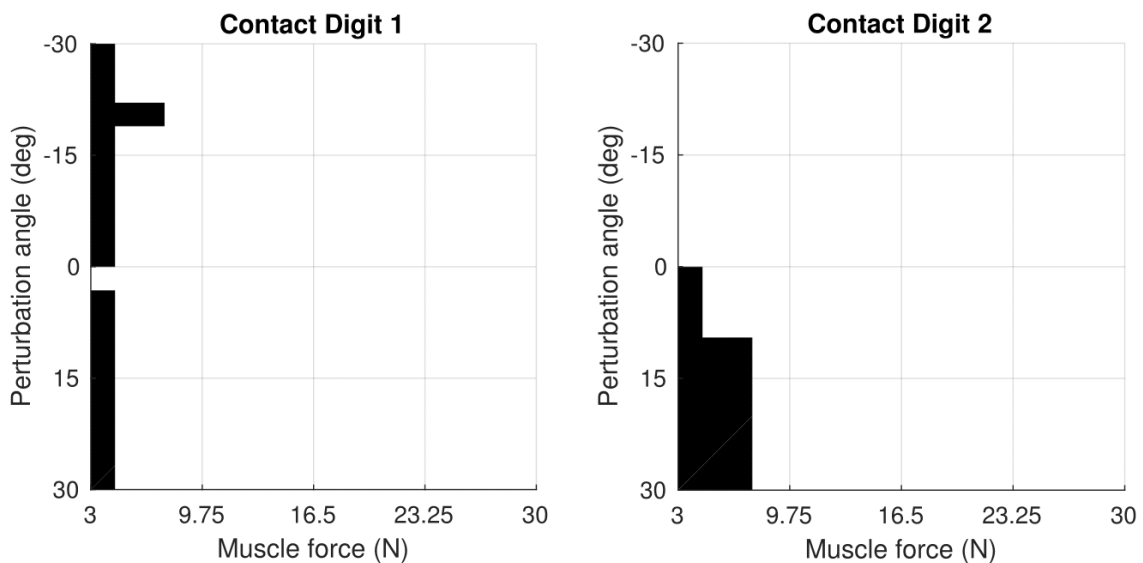


Fig.1.1H-7. The figure depicts loss of contact for each digit for 0 to 30 Newtons tendon forces at perturbation angles from 0 to ± 30 degrees when they are coupled using the implant. The panel on the left is for the index finger (digit 1) while the panel on the right is for the middle finger (digit 2). The black section denote a loss of contact while the white sections denote the maintenance of contact. Notice the minimal loss of contact when using the implant.

- Subtask 1.1I: Revise design and fabricate as needed
 - Several iterations of the implant design and fabrication were completed. Various designs for the spikes, grooves and variations in overall implant dimensions were considered.
- Subtask 1.1J: Conduct pilot cadaver tests on implant

- A hand surgeon was unavailable in the fourth quarter to conduct the cadaver studies. The pilot cadaver study will be conducted at USC in November 2017. In the meantime, the experiment protocol and the biomechanical function of the implant has been successfully verified on the robotic platform.
- Subtask 1.3A: Build relevant upper-extremity biomechanical models in OpenSim
 - Upper-extremity biomechanical simulation models have been built in OpenSim, as shown in Fig.1.3A-1.
 - An equivalent biomechanical model was also created in MATLAB

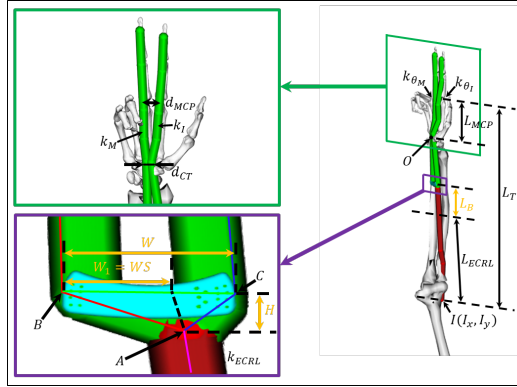


Fig.1.3A-1. OpenSim biomechanical model of Upper-extremity

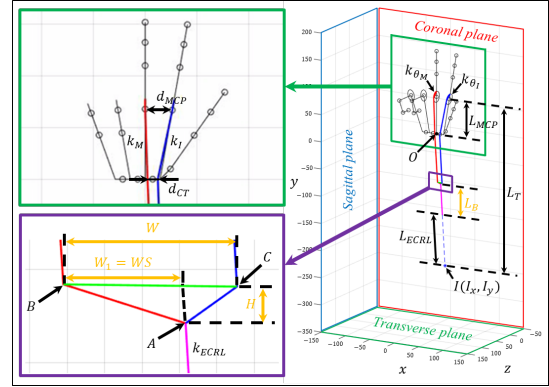


Fig.1.3A-2. Matlab model of Upper-extremity converted from OpenSim model

- The model has several variables such as FDP tendon's stiffness, distances between joints, and implant dimensions, etc. Many of these parameters are adopted from OpenSim. This model is used to identify the correct dimensions for the implant.
- Note that offsetting the implant enables the index finger to move faster and before the middle finger, which causes staggered closing of the two fingers. This enable precision fingertip grasps. This will also create larger fingertip force when contact is made.
- Subtask 1.3B: Incorporate implants into OpenSim models
 - A moving-seesaw embodiment of the implant has been created in OpenSim simulations. See figure in Subtask 1.3A and 1.3C.
- Subtask 1.3C: Develop simulations of finger movements in free space and grasping tasks
 - Simulations of the finger movements in free space and grasping tasks were developed in MATLAB. A MATLAB simulation shows the beneficial differential movement produced by the implant when compared with the conventional surgical procedure (Fig.1.3C-1). The x-axis and y-axis are parameters of the implant embodiment (the length and height of the triangle created surgically by the implant between the tendon-bifurcation). The z-axis (shading) shows the additional excursion produced by the implant. This was presented in an abstract at the Veterinary Orthopedics Society 2017 annual meeting [4].

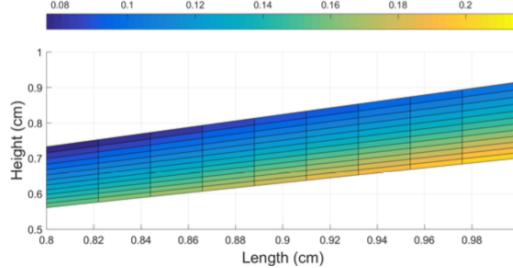


Fig.1.3C-1. Beneficial differential movement of the implant simulated via MATLAB

- In addition, a genetic algorithm was also used to analyze optimal kinematics of the muscle-tendon location, implant dimensions, and biomechanical tendon mechanism in order to maximize the differential action between the index and middle fingers. The efficacy of the implant is determined using the maximum finger flexion angle θ_{\max} , muscle contraction length L_P , and the average finger forces F_{avg} .

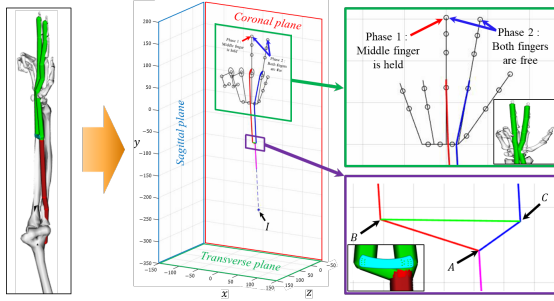


Fig.1.3C-2. The initial neutral state of the simulation for both first and second phase.

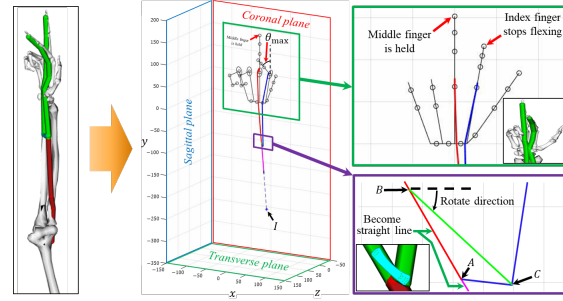


Fig.1.3C-3. The termination condition of the first phase of simulation.

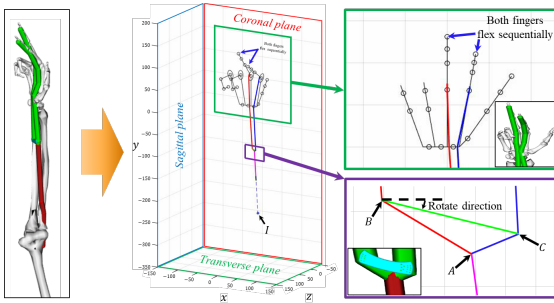


Fig.1.3C-4. An example of one moment of the simulation's second phase.

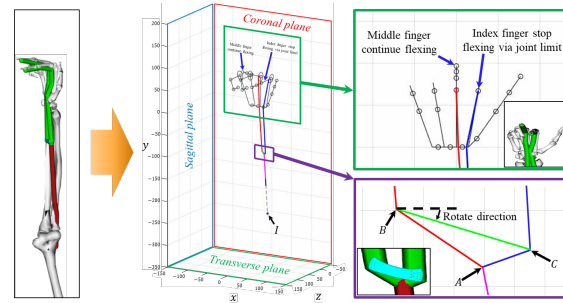


Fig.1.3C-5. The moment when index finger is stopped via joint limit.

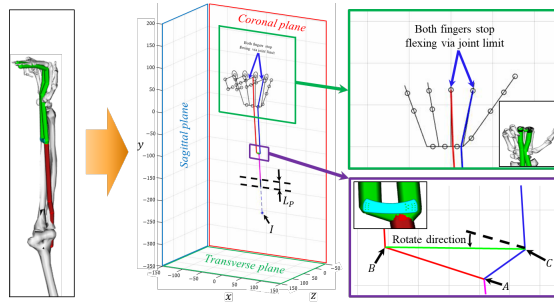


Fig.1.3C-6. The termination condition of the simulation.

- Subtask 1.3D: Identify the relationship between implant parameters and hand function enabled
 - See Subtask 1.3C above.
- Subtask 1.3E: Conduct sensitivity analysis across all implant parameters
 - The Matlab simulation described in Subtask 1.3A is used to optimize the parameters to maximize the efficiency of the implant-based technique using an 'Objective Function'

(OF)' and boundary conditions shown in Fig.1.3E-1. The elements of the objective function are as follows:

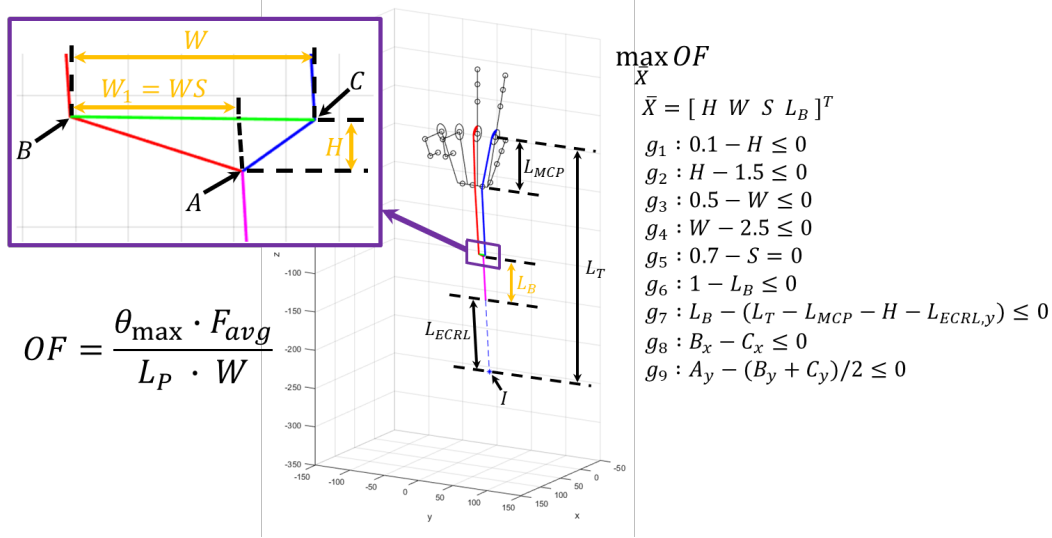


Fig.1.3E-1. Objective function equation and boundary conditions for optimization. [cm]

- θ_{\max} , the differential angle, is proportional to OF to increase the ability of the implant to provide differential action.
- F_{avg} , the average fingertip force, is proportional to OF to ensure that forces are maximized.
- L_P , the length of contraction, is inversely proportional to OF to reduce the necessary distance for the muscle to pull during full flexion of index and middle fingers.
- W , the width of the implant, is inversely proportional to OF to reduce the implants contact with the surrounding tissue and increase ease of implantation.
 - Reducing W will lower the potential differential action as shown in Fig.1.3C-1. This is useful in the objective function as the differential action is proportional to OF and high width will cause more scar tissue formation.
- The weights of parameters in the objective function will be determined with the results of the Delphi panel in Subtask 1.1B.
- The sensitivities of all implant parameters are determined using the data (red marks in Fig.1.3E-2 to 5) acquired during optimization procedure.
- The parameter L_B , the distance from the tendon origin to the bifurcation, is nonlinear to the objective function.
 - Changing L_B changes the shape of the OF interpolation map as shown in Fig.1.3E-2 to 5.
- The optimization result shows that the implant can provide largest differential action and fingertip force while minimizing the excursion of ECRL muscle when the width (W) and height (H) of the implant is 1.5mm and 0.2mm respectively.

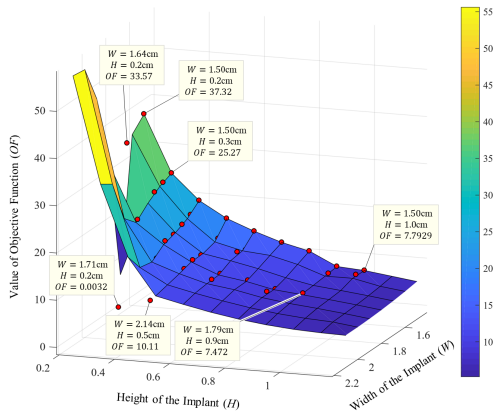


Fig.1.3E-2. The 3D interpolation plot with respect to the width (W) and height (H) of the implant, when L_B is 9.3482cm.

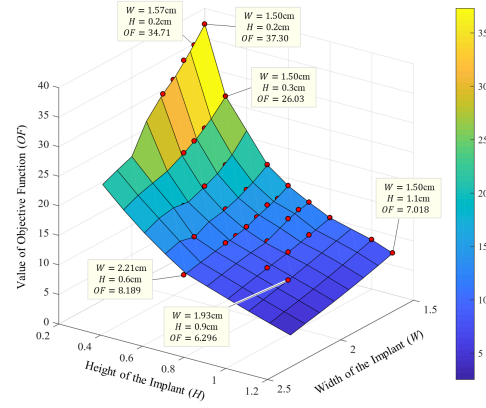


Fig.1.3E-3. The 3D interpolation plot with respect to the width (W) and height (H) of the implant, when L_B is 11.1979cm.

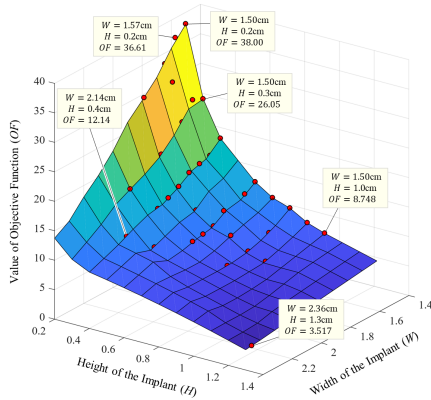


Fig.1.3E-4. The 3D interpolation plot with respect to the width (W) and height (H) of the implant, when L_B is 12.1227cm.

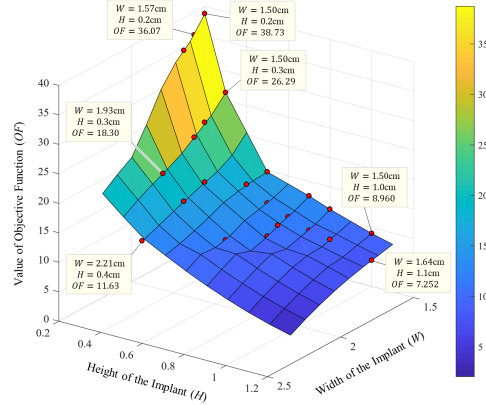


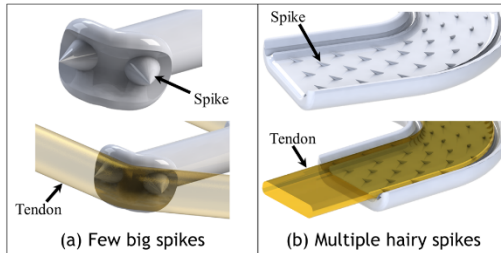
Fig.1.3E-5. The 3D interpolation plot with respect to the width (W) and height (H) of the implant, when L_B is 8.4234cm.

- Subtask 1.3F: Provide input to Task T1.1
 - Insight has been developed into how to design this implant based on the biomechanics of the muscle, tendon, and joint. Specifically, it was noticed that the primary variables that determine implant performance are its width and height. Other aspects such as the knuckle spacing or the relative position of the implant between the muscle and the knuckle also have an effect on the implant's biomechanical action, but not as significant. These must be accounted for with the same method as L_B in Subtask 1.3E.
 - We have made the implant as streamlined as possible to reduce drag from contact with surrounding tissue, reduced the number of parts, and also improved attachment between the implant and the tendon. Various adhesion techniques have also been utilized to adhere the tendon to the implant as shown in Fig 1.F. They are split into two groups, initial and long-term adhesion:

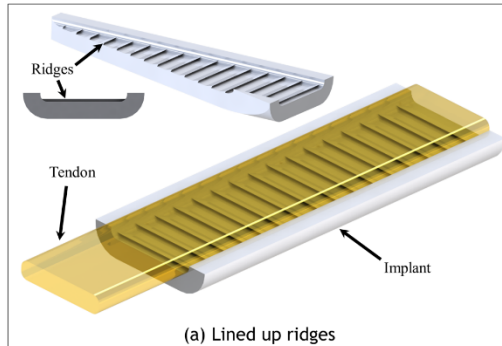
- Initial adhesion : Achieved by using spikes to bite into the tendon, tissue glue, or ridges which hold the tendon with friction due to uneven surface.
- Long-term adhesion: Achieved via spikes, pores, and channels that promote tendon growth.

Adhesion Method

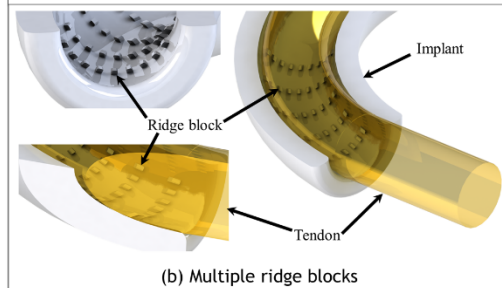
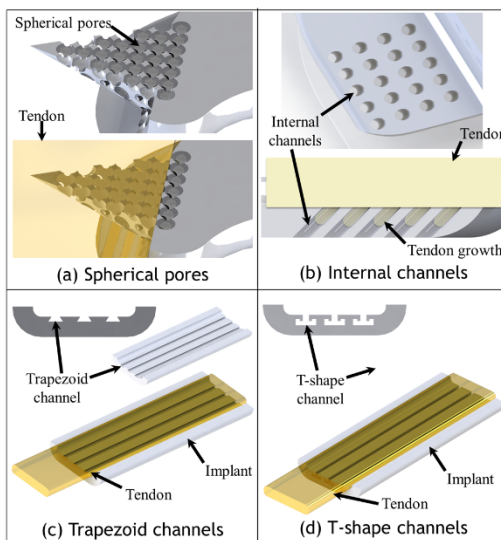
Spike



Ridge



Pore & Channel



Tissue Glue & Growth Factor

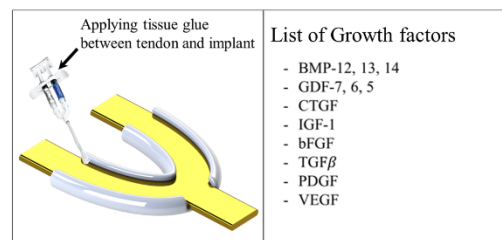


Fig. 1.3F: Methods for adhesion between tendon and implant

- Subtask 1.3G: Design cadaver experiment set-up (USC)
 - The experimental setup to actuate tendon driven robotic and cadaveric joint has been built. A computer program has been developed to control the aforementioned setup. Motion-capture and data acquisition systems have been configured to acquire, integrate and synchronize joint kinematics, tendon forces and hand configuration.

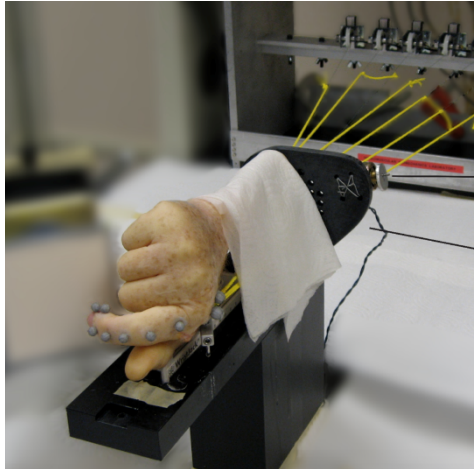


Fig.1.3G. Experimental environment of human cadaver test.

- Subtask 1.3H: Procure components for set-up (USC)
 - The necessary items have been procured.
- Subtask 1.3I: Construct set-up (USC)
 - The setup has been fully constructed and tested. See figure in subtask 1.3G.
- Subtask 1.3J: Test set-up on passive robotic fingers at OSU
 - Test set-up has been created in OSU in parallel with the testbed at USC. In the test set-up, one side of the tendon is fixed to the testbed directly and the other side is fixed to it after connecting with a spring. The spring simulates the joint stiffness of the free flexing finger when performing differential action actuated by linear servo (Servocity HDA8-50). A Linear servo controlled by a PC pulls the tendon while load cell (FUTEK LSB200 50lb) located in the middle of a kevlar string collects the applied pulling force

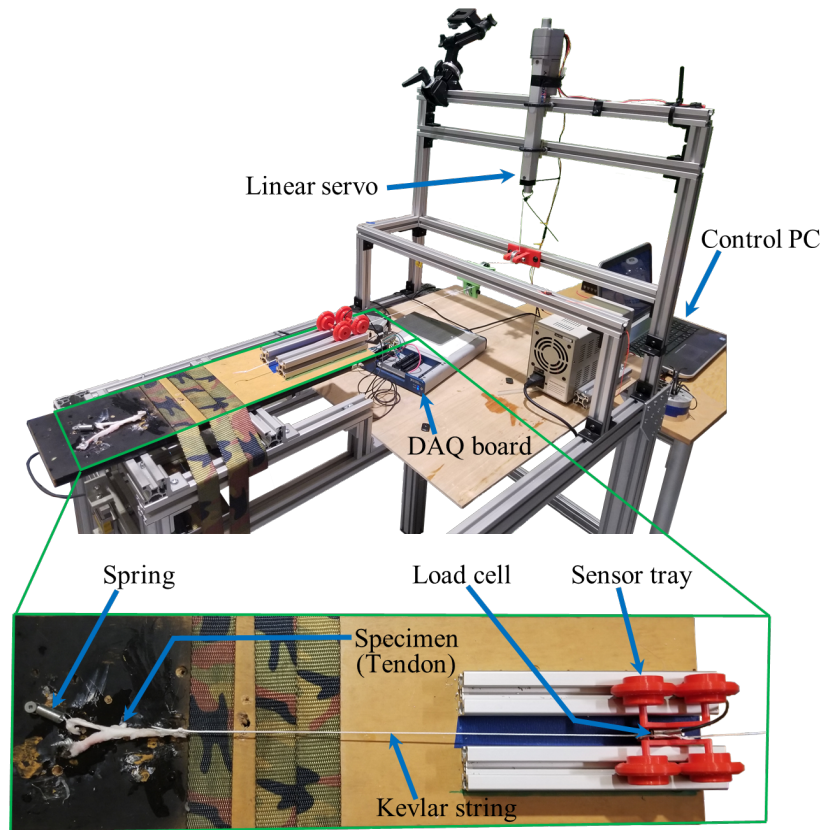


Fig.1.3J-1. Validation of test set-up on passive robotic finger composed with pig tendon and spring.

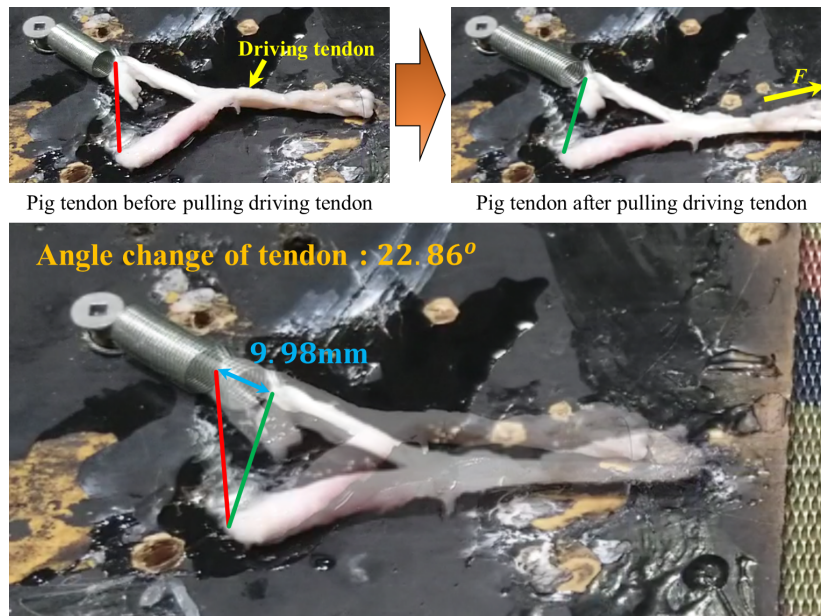


Fig.1.3J-2. Validation of test set-up on passive robotic finger composed with pig tendon and spring.

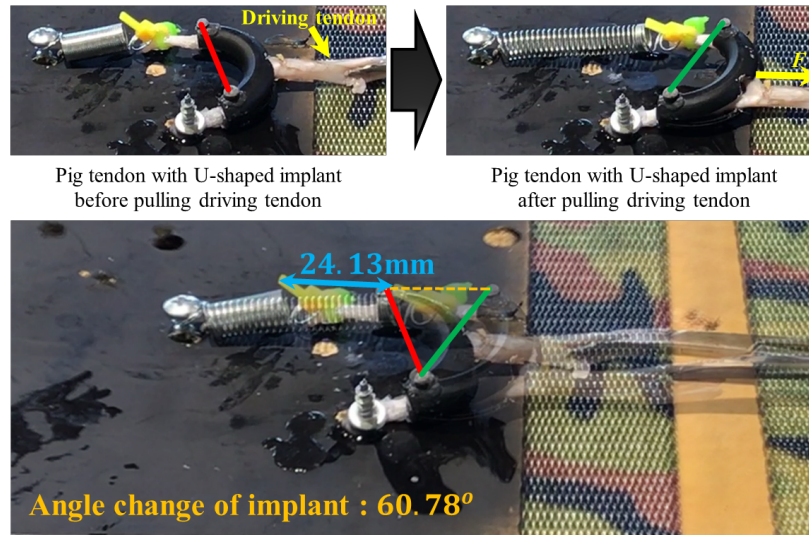


Fig.1.3J-3. Validation of the U-shaped implant using passive robotic finger

- The experiments showed that the implant-based technique produces 141.78% additional differential action when compared with the suture-based technique, as shown in Fig.1.3J-2 and 3. The maximum excursion provided by strut implant was less than the excursion produced by the U-shape implant in this experiment, since the strut implant was closer to the bifurcation point.

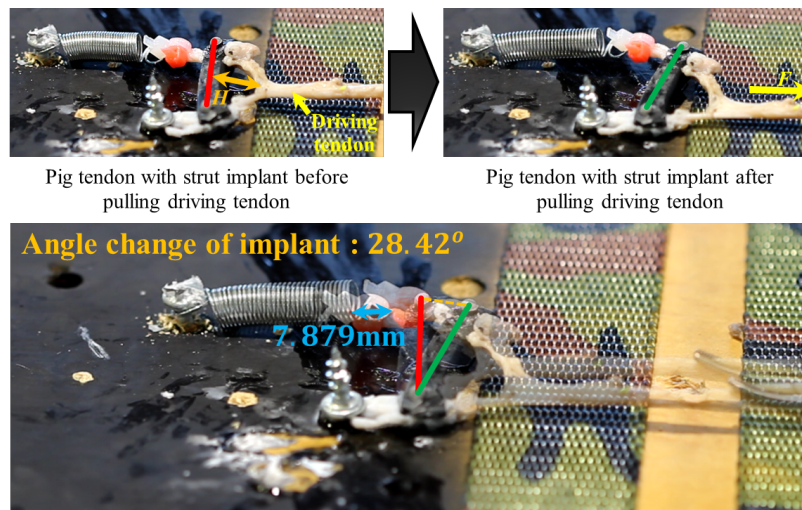


Fig.1.3J-4. Validation of the strut implant using passive robotic finger

- Subtask 1.3K: Revise set-up design and repeat test as needed
 - The trials in subtask 1.1H were conducted multiple times to achieve the result shown above.
- Subtask 1.3L: Procure first set of cadavers
 - The cadavers are being procured for the November cadaver experiment.
- Subtask 1.3M: Conduct pilot studies on cadavers to inform the design process

- The cadaver experiment will be performed in November 2017. There is a delay due to the unavailability of a hand surgeon to help conduct the surgery. In the meantime, the implant performance has been validated using a robotic testbed.
- Subtask 2.1A-2.1C: Surface activation of Kevlar/PVDF/UHMWPE with hydroxyethyl methacrylate RF-plasma
 - Surface activation of Polypropylene (material chosen for fabricating the implant) with hydroxyethyl methacrylate (PHEMA) has been achieved using Radio Frequency (RF)-plasma polymerization. The samples were cleaned using a four solvent process and then dried under laminar flow for 24 hours. The clean samples were argon etched in a plasma reactor followed by deposition of a methane layer, which aids in the adhesion of the polymer layer. The polymer vapors were then deposited on the sample surface followed by sample collection under argon, to avoid sample contamination. The results were confirmed using X-ray photoelectron spectroscopy (XPS), which is a surface analysis technique used to measure the composition of various elements present on the surface. The presence of PHEMA on the surface is measured in terms of Carbon and Oxygen percentage on the surface. 68 % Carbon and 32 % Oxygen was detected on the surface of the samples, which confirmed the presence of PHEMA. The following XPS spectra confirms the results:

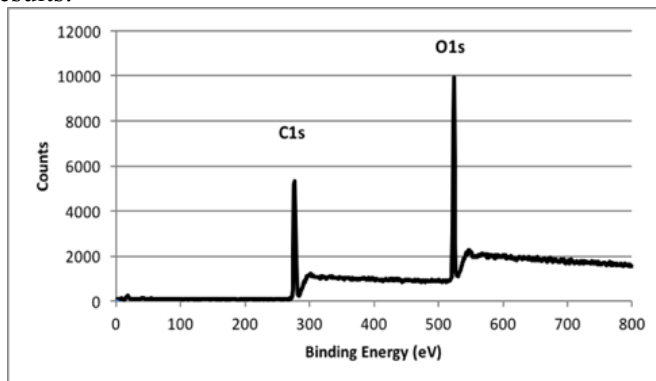
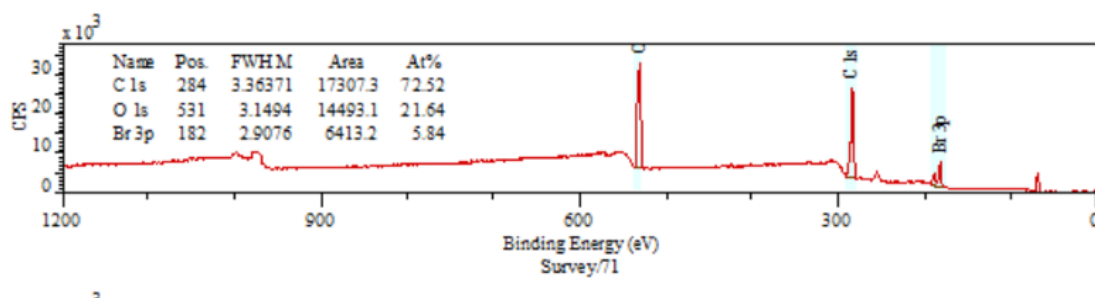


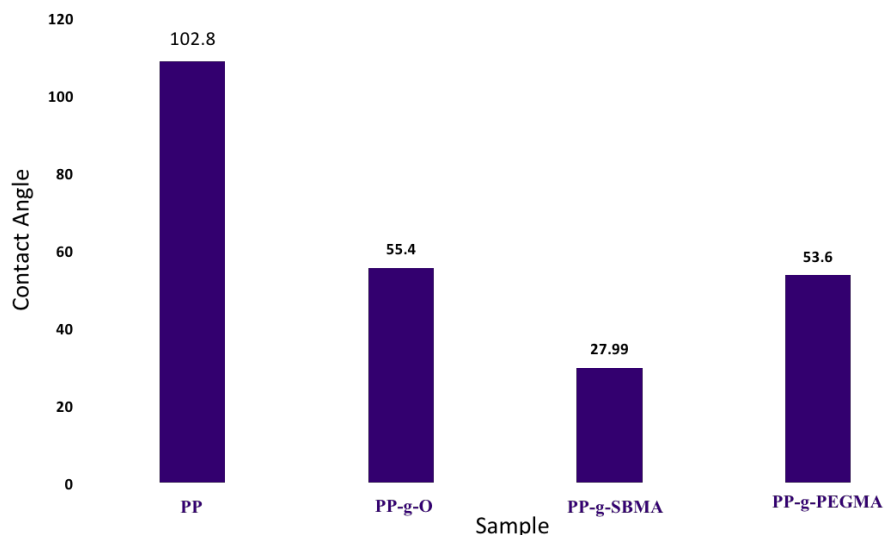
Figure : XPS survey spectra of Polypropylene substrate coated with PHEMA

The carbon (C 1s) and oxygen (O1s) peaks confirm the presence of PHEMA on the surface. PHEMA provides a layer of hydroxyl (-OH) groups on the surface, which act as a handle for further reactions.

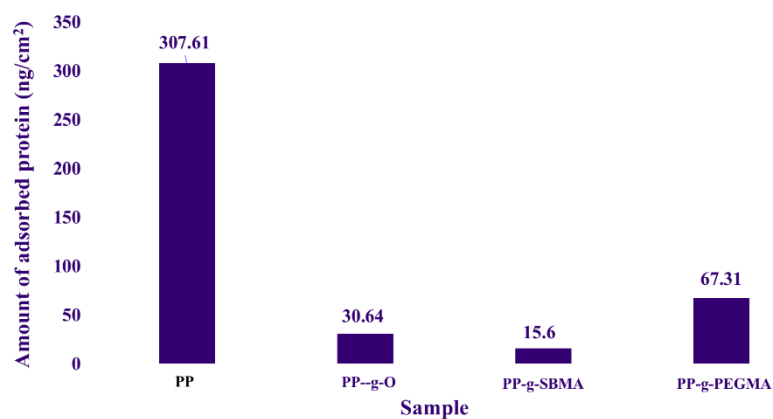
- Subtask 2.1D: Derivatization of the -OH surfaces with a RAFT or ATRP initiator
 - Derivatization of the -OH groups has been achieved using γ -Bromoisobutryl bromide (-BIBB), which is an ATRP initiator. The PHEMA coated samples were soaked in a solution of dichloromethane and BIBB for 24 hours, 6 hours at 4°C and 18 hours at room temperature. The samples were then washed with a methanol to remove wash off the unreacted reagents. A bromine density of 5.8 % was detected on the surface using XPS. The derivatization of -OH group to bromine groups confirmed the immobilization of ATRP initiator on the sample surface. The following XPS spectra confirms the presence of bromine on the surface:



- Subtask 2.1E: Growth of a brush of sulfobetaine methacrylate polymer onto the surface
 - The growth of sulfobetaine methacrylate (PSBMA) polymer brushes has been achieved on the surface using atom transfer radical (ATRP) polymerization. PSBMA is a non-fouling polymer that reduces non-specific protein adsorption on the implant surface which in turn reduces fibrosis and other effects of foreign body reactions. Copper bromide was used as a catalyst with bipyridyl as the ligand. The monomer was dissolved in the chosen solvent system and the solution was degassed thoroughly followed by the addition of the catalyst and the samples. The reaction was allowed to run for 24 hours. After the reaction termination all the samples were thoroughly washed to remove any unreacted reagents. The thickness of the coating layer was measured using an ellipsometer and was found to be around 18 nm. The team is working on increasing the coating layer thickness to around 24 nm, to further increase the non-fouling capacity of the implant surface.
- Subtask 2.1F: Surface analysis to confirm good coating quality
 - Precursory experiments to coat the biocompatible material (i.e. Polypropylene) with non-fouling polymers were conducted successfully. Some samples were analyzed for studying the coating quality. Contact angle and XPS techniques were used to study the coating quality. As can be seen in the figure below, the contact angle of PSBMA grafted Polypropylene (PP-g-SBMA) was found to around 28° which is a characteristic of hydrophilic surfaces. Hydrophilicity increases the protein resistance by avoiding non-specific protein adsorption. The contact angle for pristine Polypropylene surface was found to be 103°, which signifies a hydrophobic surface. The decrease in contact angle confirms the presence of a non-fouling coating on the surface. PEGMA and PHEMA, which are low fouling materials, were used as controls. Surfaces coated with PEGMA and PHEMA also showed hydrophilic characteristics, with contact angles less than 90°. As explained in subtask 2.C and 2.D, XPS analysis also confirmed the presence of a uniform coating on the surface. All the results were as expected, but still there is room for improvement. The team is working on improvising some of the parameters in ATRP reactions including the monomer : catalyst ratio and the solvent ratios, to further increase the thickness of the coating and enhance the hydrophilic characteristics of the surface.



- Subtask 2.1G: Stability studies in vitro to ensure that coating delamination does not occur
 - Most of the samples passed stability study. But delamination was observed in some of the samples after soaking overnight in water. Delamination resulted in a non-uniform layer of coating. This might be due to the surface roughness which decreases the adhesion tendency of the surface. Improper monomer:catalyst and solvent ratios used in the ATRP reactions can also be a reason for poorly tethered polymer brushes, which can easily get delaminated. Further experiments and analysis are being conducted to get a better understanding of this issue. Detailed surface analysis is being done to study delamination after every reaction step, to find out the reason for delamination. The team is still working on studying the stability of the coating in biologically simulated conditions, to ensure that no delamination will occur on the implanted device.
- Subtask 2.1H: Assessment of wear of the coating under mild abrasion
 - Abrasion studies still need to be done. The team does not have any data to report for this subtask.
- Subtask 2.1I: Measurement of protein resistance
 - Protein resistance was studied using Iodine-125 radiolabeling and tagging. Human serum albumin (HSA) was chosen as the protein for this study. Albumin was tagged with iodine-125 and carefully purified. The samples were soaked in the tagged protein and thoroughly washed with a buffer solution to avoid any false signals. Experiments have shown a twenty-times reduced protein adsorption on the modified samples as compared to the pristine Polypropylene samples. The coated substrates showed a protein adsorption of 15 ng/cm², in comparison to 300 ng/cm² on the unmodified PP samples.



The team is currently working on improvising the coating process protocol to further increase the protein resistance to around $<5\text{ng/cm}^2$. Increasing the hydroxyl group density and Bromine density are two suggested ways for increasing the grafting density of non-fouling polymer brushes. The grafting density can also be increased by varying the monomer:catalyst ratio and ratio of solvents used. The team is also trying out other non-fouling polymers like Carboxybetaine methacrylate (CBMA) and 2-methacryloyloxyethyl phosphorylcholine (MPC), to achieve a higher protein resistance.

Describe the Regulatory Protocol and Activity Status (if applicable).

Describe the Protocol and Activity Status for sections a-c, as applicable, using the format described for each section. If there is nothing significant to report during this reporting period, state “Nothing to Report.”

(a) Human Use Regulatory Protocols

TOTAL PROTOCOLS: *State the total number of human use protocols required to complete this project (e.g., 5 human subject research protocols will be required to complete the Statement of Work.”). If not applicable, write “No human subjects research will be performed to complete the Statement of Work.”*

“No human subjects research will be performed to complete the Statement of Work.”

(b) Use of Human Cadavers for Research Development Test & Evaluation (RDT&E), Education or Training

“Cadaver” is defined as a deceased person or portion thereof, and is synonymous with the terms “human cadaver” and “post-mortem human subject” or “PMHS.” The term includes organs, tissues, eyes, bones, arteries or other specimens obtained from an individual upon or after death. The term “cadaver” does not include portions of an individual person, such as organs, tissue or blood, that were removed while the individual was alive (for example, if a living person donated tissue for use in future research protocols, that tissue is not considered a “cadaver” under this policy, regardless of whether the donor is living or deceased at the time of tissue use).

TOTAL ACTIVITIES: 1

ACTIVITIES: *Provide the following information in a bulleted list for all RDT&E, education or training activities involving human cadavers conducted or supported during the quarter:*

- Title of the RDT&E, education or training activity
- SOW task/aim associated with the activity
- Date the activity was conducted
- Identification of the organization’s responsible individual (e.g., PI or individual primarily responsible for the activity’s conduct)
- Brief description of the use(s) of cadavers in the activity and the total number of cadavers used during the reporting period
- Brief description of the Department of Army organization’s involvement in the activity
- Status of document submission and approvals
- Problems encountered in the procurement, inventory, use, storage, transfer, transportation and disposition of cadavers used for RDT&E, education or training. Examples of problems include but are not limited to: loss of confidentiality of cadaveric donors, breach of security, significant deviation from the approved protocol, failure to comply with state laws and/or institutional policies and public relations issues.

<u>TOTAL ACTIVITIES: 1</u>

ACTIVITIES:

- Approval was obtained from the DoD and the USC for the human cadaver study titled “Design and Validation of Implantable Passive Mechanisms for Orthopedic Surgery”
- The activity involves the design, development, and validation of an implantable mechanism that will improve muscle and tendon movement.
- Tasks 1.3G—1.3S in SOW
- 26 cadavers will be used in the study.
- The cadaver experiment will be conducted in Year 2, first quarter.

(c) Animal Use Regulatory Protocols

TOTAL PROTOCOL(S):

State the total number of animal use protocols required to complete this project (e.g., 2 animal use research protocols will be required to complete the Statement of Work.). If not applicable, write “No animal use research will be performed to complete the Statement of Work.”

PROTOCOL(S):

List the identifier and title for all animal use protocols needed to complete the project. Include information about the approved target number for statistical significance, type of submission, type of approval with associated dates, and performance status. The following format shall be used:

Protocol (of total):

Protocol [ACURO Assigned Number]:

Title:

Target required for statistical significance:

Target approved for statistical significance:

Submitted to and Approved by:

Provide bullet point list of protocol development, submission, amendments, and approvals (include IACUC in addition to ACURO).

Status:

Provide bullet point list of performance and/or progress status relating to the above protocol and discuss any administrative, technical, or logistical issues that may impact performance or progress of the study (e.g. animal use protocol needs revision to minimize animal suffering, animal protocol modification to include additional staff) for the above ACURO approved protocol.

TOTAL PROTOCOL(S): 2

PROTOCOL (1 of 2 total):

Protocol [ACURO Assigned Number]: MR150091.01

Title: Biomaterials Correlation of In Vivo Histology and In Vitro Cytokine Release

Target required for statistical significance: 8

Target approved for statistical significance: 8

SUBMITTED TO AND APPROVED BY:

UW IACUC (protocol number 3043-01) and USAMRMC Animal Care and Use Review Office (ACURO)

STATUS:

PROTOCOL (2 of 2 total):

Protocol [ACURO Assigned Number]: MR150091.02

Title: Experimental Validation of Implantable Passive Mechanism in Live Animals

Target required for statistical significance: 61

Target approved for statistical significance: 61

SUBMITTED TO AND APPROVED BY:

OSU IACUC (protocol number 4775) and USAMRMC Animal Care and Use Review Office (ACURO)

STATUS:

What opportunities for training and professional development has the project provided?

- *If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."*
- *Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars no listed under major activities.*

Training:

1. Training for PI Dr. Balasubramanian
 - 1.1. Presented implant development in front of hand surgeons, biomechanics experts, and hand rehabilitation experts at the 11th Symposium of Hand and Wrist Biomechanics International at the International Society of Biomechanics 2017. Explored implant design concepts, testing protocols, conducted a Delphi panel survey with hand surgeons to identify the key metrics to evaluate the implant.
 - 1.2. Consulted with Dr. Rod Hentz, hand surgeon, on implant design and testing protocols.
 - 1.3. Consulted with Dr. Christopher Allan, hand surgeon, on implant design and testing protocols.
 - 1.4. Mentored by Dr. Buddy Ratner, co-I and biomaterials experts, on implant design, material choice, and fabrication.
 - 1.5. Mentored by Dr. Valero-Cuevas, co-I and biomechanics expert, on biomechanical testing methods.
2. Training for post-doctoral fellow Dr. Won Suk You
 - 2.1. Trained by PI on implant design, biomechanical testing, project planning
3. Training for graduate students
 - 3.1. Trained by PI and post-doctoral fellow on implant design, biomechanical testing, project planning
4. Training for undergraduate students
 - 4.1. Trained on implant design, fabrication, and biomechanical testing.
5. Presented research seminars to faculty and students at several universities including Johns Hopkins University, University of Maryland, University of Southern California, Stanford University, University of Utah, and Case Western Reserve University, University of California Los Angeles.
6. UW Graduate students: Trained by co-I on surface modification, surface analysis, biocompatibility testing, polymer synthesis, and project planning.
7. The USC graduate students and post-doctoral fellow were trained by the co-I Valero-Cuevas on biomechanical testing and the use of robotic testbeds to prepare for cadaver experiments.
8. All participants assisting in the cadaver studies at the University of Southern California have undergone General Lab Safety (GLS) training as well as Bloodborne Pathogens (BBP) training to minimize the possibility of injury, and risk of transmission of bloodborne pathogens. These trainings have also provided insights into damage mitigation in the event of an accident or injury. The BBP program also provided an opportunity for the participants to get immunization for the Hepatitis-B vaccine.

Professional development

1. The team presented papers at the following conferences

- 1.1. 11th Symposium of Hand and Wrist Biomechanics International at the International Society of Biomechanics 2017
- 1.2. The Veterinary Orthopedic Society 2017 annual meeting
- 1.3. The Military Health Systems Research Symposium 2017
- 1.4. The Orthopedic Research Society Musculoskeletal Biology Workshop 2017
- 1.5. American Society of Biomechanics 2017
- 1.6. Northwest Biomechanics Symposium 2017

How were the results disseminated to communities of interest?

- *If there is nothing significant to report during this reporting period, state "Nothing to Report."*
- *Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.*

Please mention any results disseminated to communities of interest, if applicable.

1. Results were disseminated through the conferences listed above under professional development and the research seminars listed in #5 under training.

What do you plan to do during the next reporting period to accomplish the goals and objectives?

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

1. During the next reporting period, the primary goal of this project is to develop implantable passive mechanisms for orthopedic surgery same as this reporting period.
2. Here are the subtasks that were identified in the approved SOW:
 - Subtask 1.1J: Analyze cadaver study results with clinical and commercialization partners in the team (month 13)
 - Subtask 1.1K: Revise implant design and fabricate as needed (months 13—14)
 - Subtask 1.1M: Revise implant design based on full cadaver study (months 23—24)
 - Subtask 1.3F: Provide input to Task T1.1 (months 13—14)
 - Subtask 1.3N: Procure second set of cadavers (month 13)
 - Subtask 1.3O: Re-assemble set-up (month 15)
 - Subtask 1.3P: Coordinate with clinical partners the metrics of success for cadaver studies (month 16)
 - Subtask 1.3Q: Conduct cadaver experiments (months 17—18)
 - Subtask 1.3R: Analyze data (months 19—21)
 - Subtask 1.3S: Feedback results to Tasks T1.1 and T1.2 (month 22)
 - Subtask 1.3T: Coordinate with clinical partners the metrics of success for live animal studies (month 20)
 - Subtask 2.1I: Measurement of protein resistance (months 10—15)
 - Subtask 2.2A: Prepare specimens for implantation (months 13—14)
 - Subtask 2.2B: Test for endotoxin and extractables (months 14—16)
 - Subtask 2.2C: Implant in mice (months 17—22)
 - Subtask 2.2D: Harvest implants and fix samples (months 18—23)
 - Subtask 2.2E: Embedding, staining, and sectioning (months 19—23)
 - Subtask 2.2F: Histological analysis and measurement by microscopy (months 20—24)

4. IMPACT: *Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:*

What was the impact on the development of the principal discipline(s) of the project?

- *If there is nothing significant to report during this reporting period, state “Nothing to Report.”*
- *Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the vase of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).*

This project has made distinctive contributions as follows:

1. In the domain of orthopedic surgery, the work has brought to the attention of numerous surgeons and hand therapists the possibility of a paradigm shift in orthopedic surgery.
2. In the domain of implant design and fabrication, the work is developing new techniques for implant fabrication (3D printing) and enabling attachment between an artificial implant and a biological tendon.
3. In the domain of experiments with robotic testbeds and animal cadavers, this is the first time such experiments are conducted with robotic testbeds and cadavers where implants are inserted between tendons to modify and improve force and movement transmission.
4. In the domain of live-animal experiments, this is the first time such experiments are conducted with live animals where implants are inserted between tendons to modify and improve force and movement transmission.
5. In the domain of developing non-fouling implant coatings, this works develops non-fouling and lubricious polymer coatings for implants that slide between layers of tissue.

What was the impact on other disciplines?

- *If there is nothing significant to report during this reporting period, state “Nothing to Report.”*
- *Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on other disciplines.*

This work has created a new application are for the domains of robotics and mechanism design.

Specifically, the robotics domain has primarily focused on developing devices outside the human body, such as orthoses, exoskeletons, and prostheses. This work opens up the possibility of designing robotic devices for within the body. Similarly, the mechanism design domain has primarily designed mechanisms such as four-bar linkages, and pulleys for artificial mechanical devices. This work opens up the possibility of designing mechanisms to mesh with the human body.

What was the impact on technology transfer?

- *If there is nothing significant to report during this reporting period, state “Nothing to Report.”*
- *Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:*
 - *Transfer of results to entities in government or industry;*
 - *Instances where the research has led to the initiation of a start-up company; or*
 - *Adoption of new practices.*

- This work will likely lead to the adoption of new orthopedic surgical procedures that uses implantable mechanisms.

What was the impact on society beyond science and technology?

- *If there is nothing significant to report during this reporting period, state “Nothing to Report.”*
- *Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:*
 - *Improving public knowledge, attitudes, skills, and abilities;*
 - *Changing behavior, practices, decision making, policies (including regulatory policies), or social action; or*
 - *Improving social, economic, civic, or environmental conditions.*

- The PI has received several emails from the public expressing interest in the implant technology and expressing hope that this technology will aid their medical condition.

- 5. CHANGES/PROBLEMS:** *The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:*

Changes in approach and reasons for change

Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

1. The team has decided to use Reinforced Polyurethane as the implant material. This is because the material can be 3D printed, and 3D printing is required to achieve sufficient resolution.

Actual or anticipated problems or delays and actions or plans to resolve them

Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

1. Due to the unavailability of the hand surgeons and their residents, we were unable to conduct the cadaver studies during the fourth Quarter. The cadaver study will be conducted by USC in November 2017.
2. Since RPU is an industrial grade material and not medical grade, thorough bulk cleaning is required in addition to the surface modification. Bulk impurities can leach out and cause foreign body reactions when implanted in vivo. UW is working on finding a solution for this problem.
3. RPU swells up in almost all the solvents that can be used in various steps of ATRP reactions, which changes the product dimensions by around 16%. The swelling also significantly reduces the mechanical strength of the material, which is another potential issue. UW is conducting further experiments and analysis to fix this problem. The team is looking into different solvent combinations and also new polymerization techniques to fix this issue.

Changes that had a significant impact on expenditures

Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

- The sub-contract to UW and USC were set up one quarter after the original start date. Thus, their expenditures are reduced by a quarter.
- USC also has not yet bought the human cadavers for the cadaver experiments. So those expenditures are reduced.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

Nothing to Report

Significant changes in use or care of vertebrate animals.

ACUP approvals were obtained for a change in the number of animals required and a change in the surgical procedure.

Significant changes in use of biohazards and/or select agents

- Nothing to report.

6. PRODUCTS: List any products resulting from the project during the reporting period. If there are no products to report for the current quarter, state “Nothing to report.”

Publications, conference papers, and presentations

Report only the major publication(s) resulting from the work under this award.

- **Journal publications.** List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).
 - **Books or other non-periodical, one-time publications.** Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: Author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).
 - **Other publications, conference papers, and presentations.** Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.
1. Casebier, Justin; Mandich, Jacob; Francis, James; Chandramouli, Sushruta; Balasubramanian, Ravi; Warnock, Jennifer. Implantable Mechanisms for Orthopedic Surgery: Validation using Biomechanical Simulation and Cadaver Study in Chicken Foot. In *Proc. Veterinary Orthopedics Society*, 2017.
 2. Le, J. Casebier, J. Mandich, M. K. Larson, J. Warnock, J. Sweeney, R. Balasubramanian. Evaluation of Postoperative Healing for Novel Tendon-Transfer Surgery Using an Implantable Passive Mechanism: A Pilot In Vivo Study. In *Proc. Veterinary Orthopedics Society*, 2017.
 3. Anthony Le, Duncan S. Russell, Maureen K. Larson, Jennifer Warnock, Geoffrey R. Browning, Kay A. Fischer, James Sweeney, and Ravi Balasubramanian. Histopathological Analysis of Healing Responses to a Novel Tendon Transfer Surgery in a Chicken Model. In *Proc. ORS 47th International Musculoskeletal Biology Workshop*, 2017. (Blue Ribbon Poster award)
 4. Ravi Balasubramanian and Francisco Valero-Cuevas. Implantable passive mechanisms for differentially distributing movement across multiple tendons in tendon-transfer surgery. In *Proc. Hand Wrist Biomechanics International Workshop* held at the *International Society of Biomechanics*, 2017.
 5. Anthony Le, Duncan S. Russell, Jennifer Warnock, Maureen K. Larson, Geoffrey R. Browning, Kay A. Fischer, James Sweeney, and Ravi Balasubramanian. Histopathological Healing Responses to a Novel Tendon-Transfer Surgery in a Chicken Model In *Military Health System Research Symposium*, 2017.
 6. Won Suk You, Justin Casebier, Ravi Balasubramanian. Design of a Mechanically Anchoring Implantable Mechanism for Tendon Transfer Surgery. In *Proc. The 13th Annual Northwest Biomechanics Symposium*, 2017.

Website(s) or other Internet site(s)

List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Technologies or techniques

Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be shared.

- This work will lead to the development of implantable mechanisms and non-fouling coatings for implants.
- This work will lead to the development of new surgical techniques that utilize the developed implants.

Inventions, patent applications, and/or licenses

Identify inventions, patent applications with date, and/or licenses that have resulted from the research. State whether an application is provisional or non-provisional and indicate the application number. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Provisional Patent 14/725,971 “Implanted Passive Engineered Mechanisms And Methods For Their Use And Manufacture” is under review.

Other products

Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment, and/or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

- data or databases;
- biospecimen collections;
- audio or video products;
- software;
- models;
- educational aids or curricula;
- instruments or equipment;
- research material (e.g., Germplasm; cell lines, DNA probes, animal models);
- clinical interventions;
- new business creation; and
- other.

Nothing to report.

7. PARTICIPANTS & OTHER ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."

Name: Ravi Balasubramanian
Project Role: PI
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 0.375
Contribution to Project: Planning and technical lead for project and for work at OSU

Name: Jennifer Warnock
Project Role: Co-I
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 0.3375
Contribution to Project: Surgical lead for live-animal work at OSU

Name: James Sweeney
Project Role: Co-I
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 0.0125
Contribution to Project: Lead for live-animal Functional Electrical Stimulation work at OSU

Name: Francisco Valero-Cuevas
Project Role: Co-I
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 0.125
Contribution to Project: Planning and technical lead for work at USC

Name: Buddy Ratner
Project Role: Co-I
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 0.15
Contribution to Project: Planning and technical lead for work at UW

Name: Forrest Ling
Project Role: Project Manager
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 0.5
Contribution to Project: Project coordination and logistics

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

- *If there is nothing significant to report during this reporting period, state "Nothing to Report."*
- *If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.*

1. Consultant Dr. Cho withdrew from the project.

- In place of Dr. Cho, Dr. Vincent R. Hentz, Former Head of Hand Surgery and now Staff Surgeon at the VA Palo Alto Health Care System, has agreed to be the surgeon-collaborator on this project. He is one of the world's top experts in upper-extremity tendon transfers and a long-time collaborator of Dr. Valero-Cuevas, a Co-Investigator on this project.
- The PI has prepared a revised Statement of Work with Dr. Hentz in place of Dr. Cho and submitted the Statement of Work with the April quarterly report.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

- *If there is nothing significant to report during this reporting period, state "Nothing to Report."*
- *Describe partner organizations - academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) - that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.*

Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: *For collaborative awards, independent reports are required from BOTH the Initiating PI and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to <https://ers.amedd.army.mil> for each unique award.*

QUAD CHARTS: *If applicable, the Quad Chart (available on <https://www.usamraa.army.mil>) should be updated and submitted with attachments.*

Quad chart attached to report.

9. **APPENDICES** : *Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc. Reminder: Pages shall be consecutively numbered throughout the report. DO NOT RENUMBER PAGES IN THE APPENDICES.*

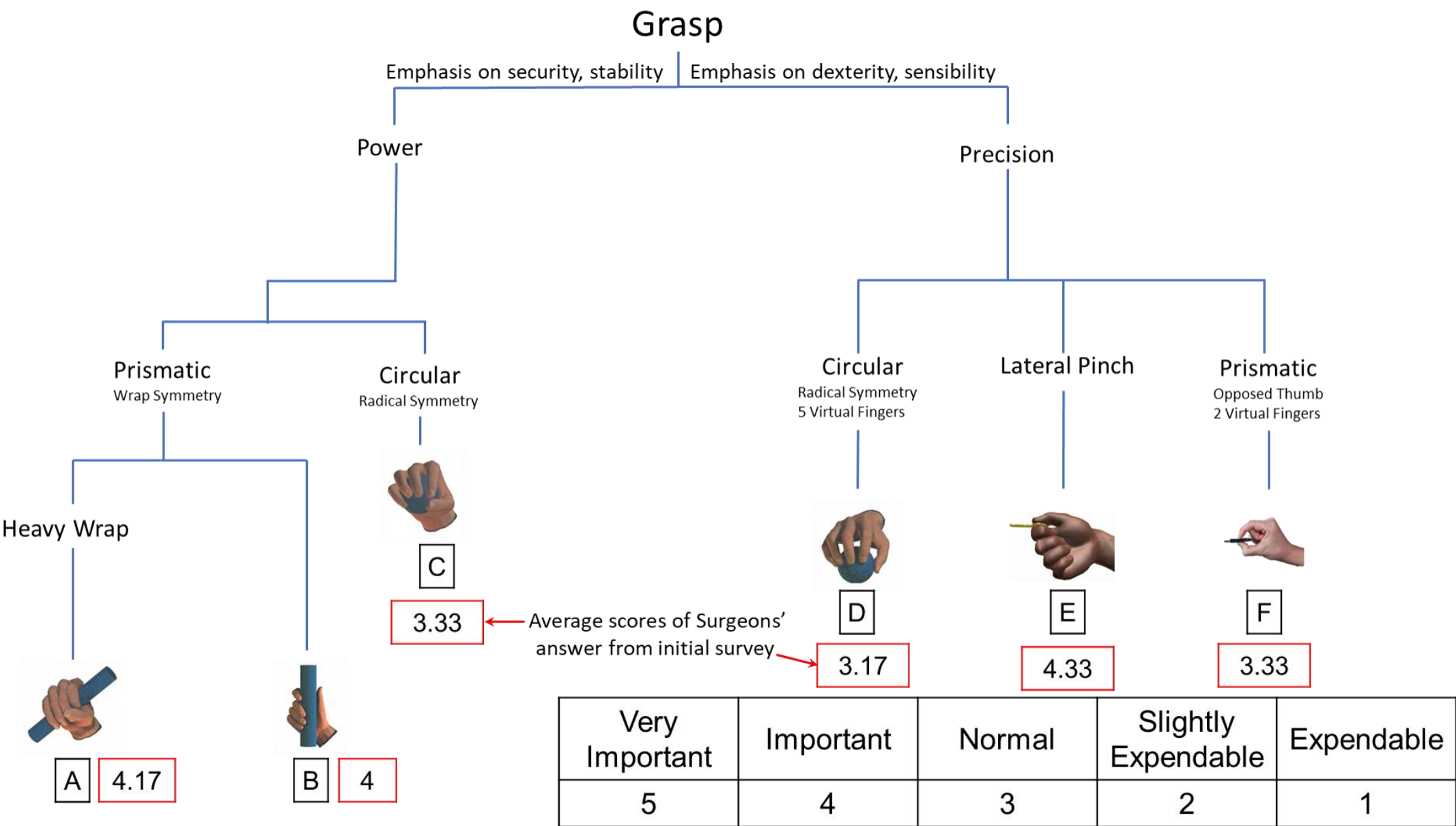
The appendix includes the Delphi Panel survey conducted with hand surgeons and hand rehabilitation experts and all the publications from this period

<REFERENCES>

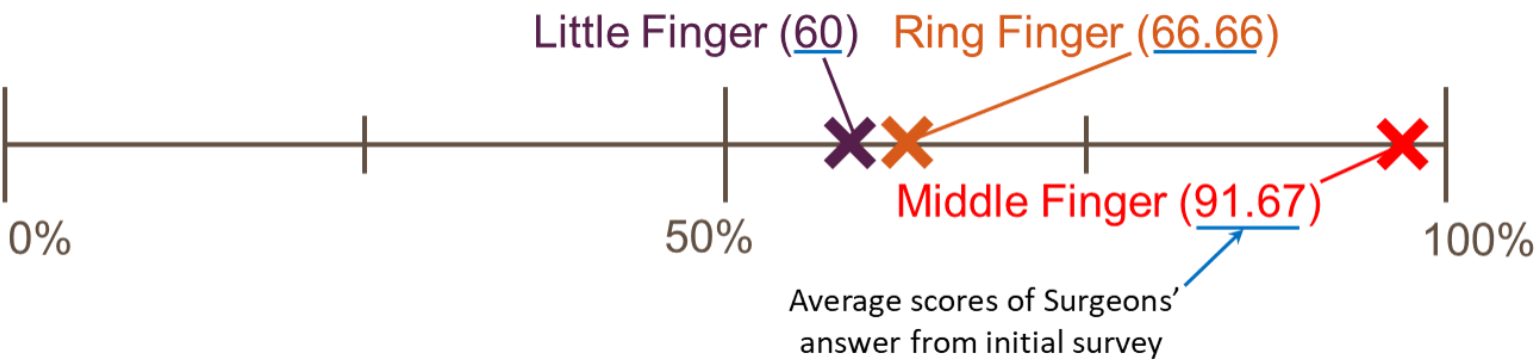
1. S. Jacobsen, E. Iversen, D. Knutti, R. Johnson and K. Biggers, Design of the Utah/M.I.T. Dextrous Hand, In *Proc. IEEE International Conference on Robotics and Automation*, pp. 1520-1532, 1986
2. K. Mardula, R. Balasubramanian and C. H. Allan, Implanted passive engineering mechanism improves hand function after tendon transfer surgery: A cadaver-based study, *HAND*, vol. 10, no. 1, pp. 116-122, 2015.
3. T. Homayouni, K. N. Underwood, K. C. Beyer, E. R. Martin, C. H. Allan, and R. Balasubramanian, Modeling Implantable Passive Mechanisms for Modifying the Transmission of Forces and Movements Between Muscle and Tendons, *IEEE Transactions on Biomedical Engineering*, vol. 62, no. 9, pp. 2208-2214, 2015
4. Le, J. Casebier, J. Mandich, M. K. Larson, J. Warnock, J. Sweeney, R. Balasubramanian. Evaluation of Postoperative Healing for Novel Tendon-Transfer Surgery Using an Implantable Passive Mechanism: A Pilot In Vivo Study. In *Proc. Veterinary Orthopedics Society*, 2017.

Metrics for Bio-Mechanic Hand Function

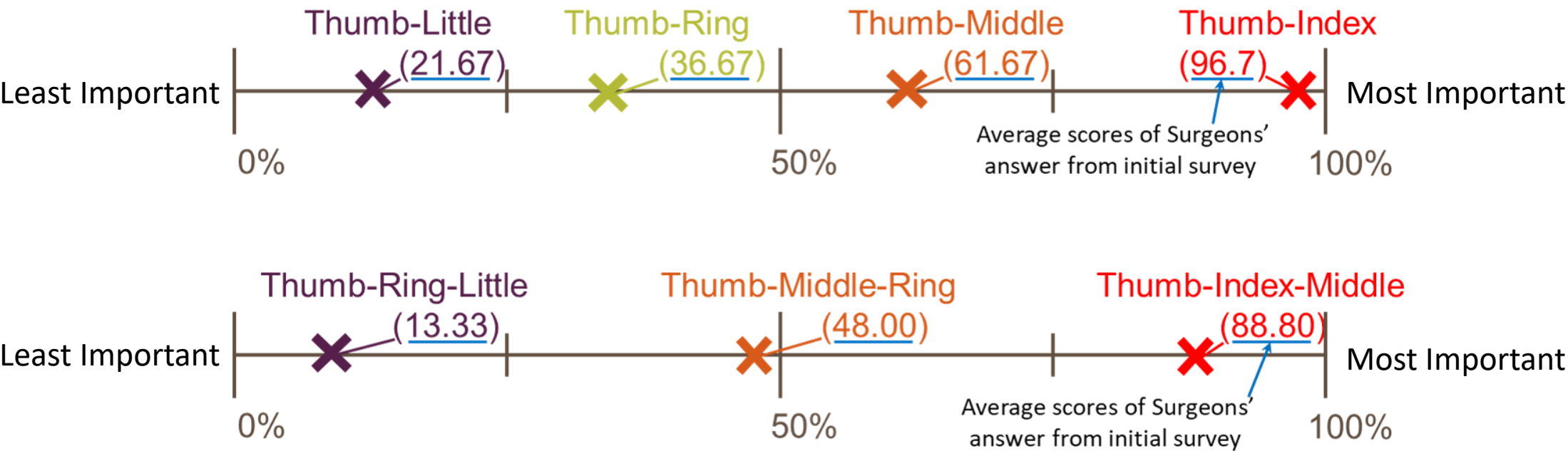
1. Power grasp vs. Precision grasp: What types of grasps would you (as a surgeon) like for high median-ulnar nerve palsy patients to have post-surgery? Please put the designated grading next to each picture.



2. When comparing to the force applied by the index finger, what percentage of fingertip force should the other fingers exhibit? (Assuming the index finger is the strongest)



How Important is each type of precision (fingertip) grasp to hand function in daily activities?



3. How would you score the importance of each factor in a power grasp?

Factor 1:Maximum grasping force	➤ Factor 1: A 3.66
Factor 2:How long can power grasp be held with max force	➤ Factor 2: B 4.17

Very Important	Important	Normal	Slightly Expendable	Expendable
5	4	3	2	1

4. For patients with high median-ulnar palsy, score these objects based on their frequency of daily use.

Object 1:Cup			➤ Object 1: A	3.67
Object 2:Mobile Phone			➤ Object 2: B	3.83
Object 3:Toothbrush			➤ Object 3: C	2.33
Object 4:Hair Brush			➤ Object 4: D	2.33

More than 20 times a day	More than 10 times a day	More than 5 times a day	More than 20 times a day	Almost never used
5	4	3	2	1

5. Score the animal models on their applicability for researching tendon-transfer surgery for median ulnar palsy

Animal 1: Chicken	➤ Animal 1:	A	3.17
Animal 2: Pig	➤ Animal 2:	B	2.83
Animal 3: Horse	➤ Animal 3:	C	1.5
Animal 4: Monkey	➤ Animal 4:	D	4.33

Very Applicable	Applicable	Partially Applicable	Unsuitable	Very Unsuitable
5	4	3	2	1

6. Rate these methods on their usefulness for predicting potential finger movement and hand flexion that the patient will have post-surgery for high median-ulnar nerve palsy

Method 1: Check tenodesis effect of wrist extension on finger flexion		➤ Method 1: <input type="text" value="A"/>		
Method 2: Injury time and injury pattern		➤ Method 2: <input type="text" value="B"/>		
Method 3: Via range of motion of the wrist		➤ Method 3: <input type="text" value="C"/>		

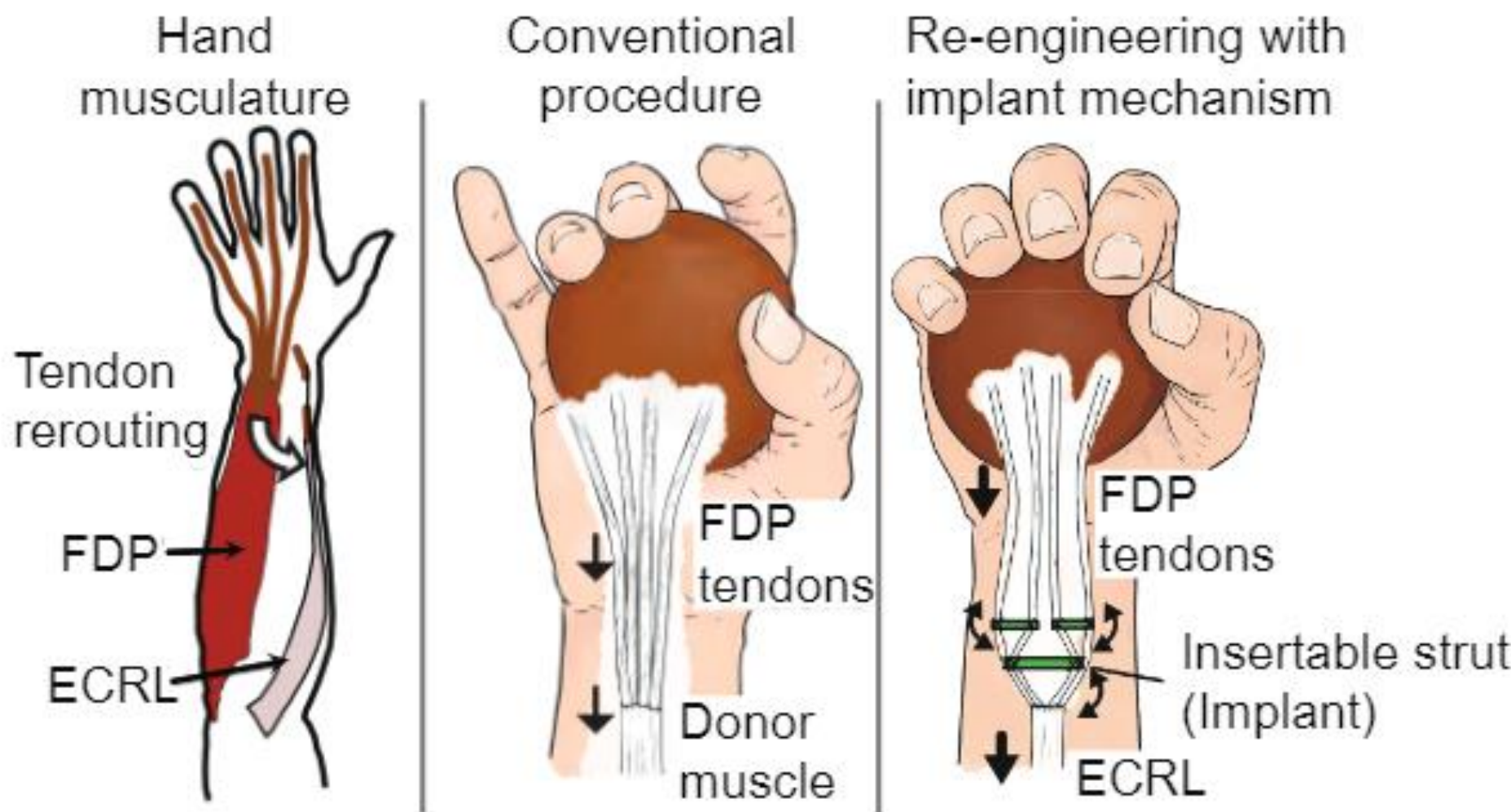
Extremely Useful	Very Useful	Useful	Slightly Useful	Not Useful
5	4	3	2	1

7. List methods that are useful for evaluating a patient's hand function before and after tendon-transfer surgery

Method 1: <u>Assessment of finger position, motion and strength</u>
Method 2: <u>Recovery of daily activities</u>
Method 3: <u>Physical exam</u>
Method 4: <u>Check passive range in wrist and digits.</u>
Method 5: <u>History and physical exam.</u>
Method 6: <u>Assess active and passive ROM</u>
Method 7: <u>Grip & pinch strength</u>
Method 8: <u>Check sensation and soft tissue</u>

Metrics for Implant Bio-Mechanical Function

For all the following questions, please consider a passive strut that will be inserted between the flexor tendons to create adaptive movement between the fingers even though they are driven by one muscle.



1. Score the importance of each factor in designing a passive mechanical implant

➤ Improved differential action	A	3.66
➤ Maximum fingertip forces	B	4
➤ Balanced distribution of fingertip forces	C	4.33
▪ Unbalanced fingertip forces will result in sequentially movement of fingers		
➤ Higher grasp quality.....	D	3.83
➤ Smaller muscle force required to establish contact	E	4.16
(No difference in finger movement in free space)		
➤ Low Resistance force due to implant	F	4.25
▪ Biologically or mechanically		

Very Important	Important	Normal	Slightly Expendable	Expendable
5	4	3	2	1

2. List subjective blind methods a surgeon or rehab expert would use to evaluate finger/toe movement following the proposed surgery

- Method 1: Able to make composite fist

Method 2: Active range of motions

Method 3: Write ones signatures

Method 4: Grip strength

Method 5: Count to “5” on fingers

Method 6: Pinch strength

3. Score the importance of each factor created by a passive mechanical implant

- Improved robustness of surgical differences (Tendon too long/short)

A

4.4

➤ Action of antagonist muscle unaffected.....

B

4.2

➤ Reduce injury to surrounding tissue

C

4.6

➤ Order of surgery immaterial to performance

D

2.2

Very Important	Important	Normal	Slightly Expendable	Expendable
5	4	3	2	1

Metrics for Measuring Patient's Hand-function Progress Post-Surgery

1. List useful evaluation methods to monitor healing post surgery

Method 1: Physical exam(Ultrasound,MRI)

Method 2: Function abilities

Method 3: Wound check

Method 4: Range of motion

Method 5: Strength

2. What symptoms are useful for gauging whether another surgery is needed?

Symptom 1: Finger motion

Symptom 2: Stiffness

Symptom 3: Lack of sensation

Symptom 4: Inability to perform daily activities

Symptom 5: Patient satisfaction/complaint
Regarding functional improvement

Symptom 6: Functional range of motion

Symptom 7: Evidence that transfer has either
Scarred down or ruptured

3. What non-invasive procedures do you find useful for checking the amount of scar tissue formation

Procedure 1: Sonography

Procedure 2: Ultrasound

Procedure 3: MRI

Procedure 4: Tenodesis

Procedure 5: No direct measure of scar
tissue only range of motion matters

Implantable Mechanisms for Orthopedic Surgery: Validation using Biomechanical Simulation and Cadaver Study in Chicken Foot

INTRODUCTION

Current surgical methods use sutures and staples to attach tissues together. However, these methods pose disadvantages when used in reconstructive orthopedic surgeries that attach multiple tendons to a single muscle. For example, the tendon-transfer surgery for high median-ulnar palsy directly sutures four finger flexor tendons to one muscle in order to restore finger flexion capability. This surgery couples the movement of all the fingers. As a result, the surgery limits hand function in physical interaction tasks such as grasping, since the fingers cannot adapt naturally to the object's shape [1]. In previous work, it has been shown using a human cadaver study that an implantable passive mechanism, such as a pulley or a link, can be used in this tendon-transfer surgery to construct a differential mechanism between the biological tendons and the actuating muscle. This differential mechanism allows for multiple fingers to move differentially and create multi-fingered grasps that can securely grab and object even when actuated by one muscle. This is because of passive translation and rotation of the implant to accommodate the difference in movement between the fingers. This contrasts with the coupled finger motion produced by the current suture-based procedure (Figure 1) [2]. This paper seeks to validate the chicken toe extensor mechanism as a model for studying this implant as we prepare to study this new surgical procedure in live animals and live humans. Specifically, the chicken foot extensor mechanism is comparable to the human hand flexor mechanism after the current surgery. The paper presents a biomechanical analysis and a cadaveric chicken foot based study of the advantage of the using the implant-based procedure in the chicken foot.

METHODS

The chicken extensor tendon mechanism and its movement is modeled in a custom-developed biomechanical simulation program in MATLAB. The tendons were modeled as spring with Young's Modulus 1.2 GPa [4]. To simulate the implant-based surgery, the implant is inserted distal of the first bifurcation point of the Extensor Digitorum Longus tendon in order to create a "triangle" using the biological tendons and the implant. To observe the differential action between

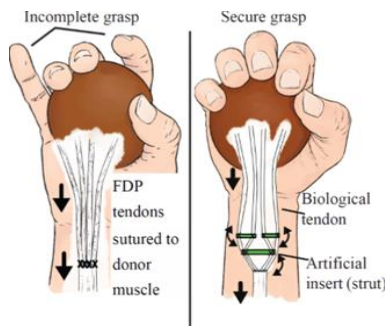


Figure 1: Tendon transfer surgery for median-ulnar nerve palsy

the toes, the medial and intermediate toes are held in a fixed position and the lateral toe is allowed to move. The extensor muscle is then contracted slowly (one millimeter at a time) (Δ_0), and the resulting toe movement of the unrestricted toe is measured. The toe movement is reported as the change in arc length (Δ_3) of the unrestricted toe enabled by the implantable mechanism (Figure 2).

The implant insertion location (from the bifurcation point) and implant length were varied to evaluate how these parameters affect output arc length.

In order to experimentally validate the implant-based procedure, the toe movement was also studied in chicken cadavers. The extensor tendons of chicken feet with and without 3D printed implants were attached to a linear actuator to simulate EDL muscle contractions. As in the simulation, differential action was simulated by holding two of the toes while the third was left unrestricted. Motion-capture cameras were utilized to measure the angular travel of the free toe (Figure 3).

RESULTS AND DISCUSSION

The biomechanical simulations showed that the differential action increased with the width of the implant and decreased with the height of the triangle. An implant with dimensions $h=0.6934$ cm, $l= 0.99$ cm showed 135% improvement in differential action when compared with the control case (Figure 4). In the cadaver study, the implanted-based procedure provided an 109% increase in angular travel of the lateral toe (Angular travel $22.36^\circ \pm 1.36^\circ$ for implanted feet, $10.67^\circ \pm 1.18^\circ$ for natural feet, $p<0.05$, $N=6$ feet for each group).

CONCLUSIONS

The increase in differential movement in the simulation and cadaver study illustrates the significant advantage of using passive implantable devices when connecting one muscle to multiple tendons as compared to the suture based procedure. This success will be demonstrated in a live chicken and later on, in the human hand.

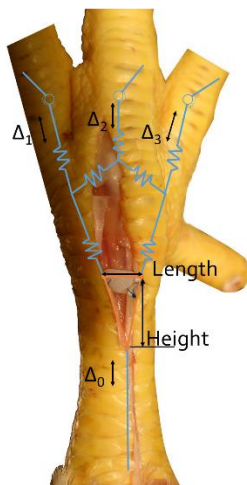


Figure 2: Tendon Network Modeled as spring system

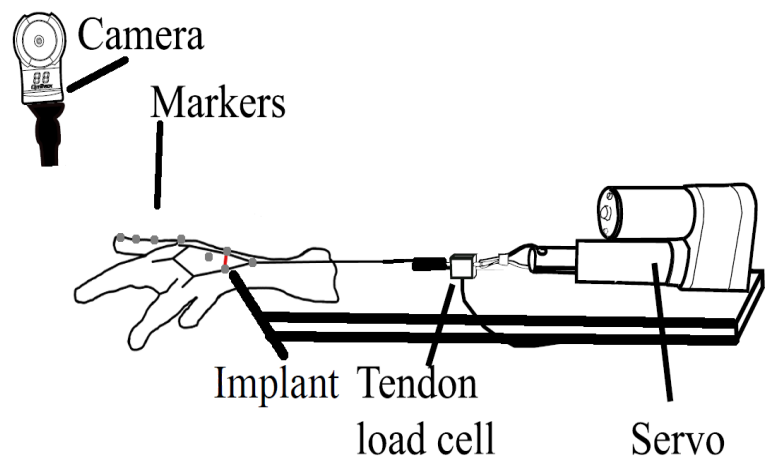


Figure 3: Experimental set-up.

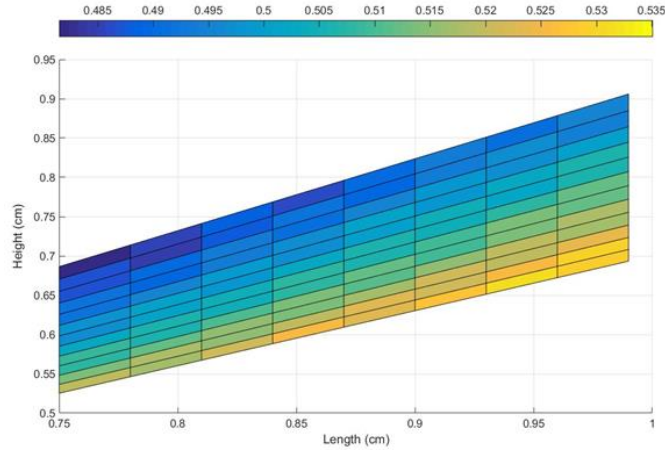


Figure 4: Arc Length for given triangle parameters

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EVALUATION OF POSTOPERATIVE HEALING FOR NOVEL TENDON-TRANSFER SURGERY USING AN IMPLANTABLE PASSIVE MECHANISM: A PILOT *IN VIVO* STUDY

Introduction: Conventional tendon-transfer surgeries involve re-routing tendons from a dysfunctional muscle to a functional one using sutures with the goal of restoring joint function [1][3]. However, sutures are only capable of directly coupling the muscle and tendon movements (Figure 1a). They cannot scale or distribute the muscle's force and movement across the tendons. This becomes a problem in, for example, the tendon-transfer surgery for high-median ulnar nerve palsy, where multiple finger flexor tendons are directly re-routed from the Flexor Digitorum Profundus (FDP) muscle bellies and sutured to the one Extensor Carpi Radialis Longus (ECRL) muscle belly (Figure 1c) [3]. While this procedure is simple, it couples the finger movements and prevents them from individually adapting to an object's shape during grasping tasks. To address this problem, our group is developing a new surgical procedure that constructs a differential mechanism in-situ in the forearm using the biological tendons and implantable passive elements as an alternative to the suture-based tendon-transfer surgery (Figure 1b) [5][6]. The implant for this surgery was a miniature artificial link, dubbed the implantable passive mechanism. Our previous studies using biomechanical simulations and human and chicken cadavers have shown that the implant-based surgery significantly improves the adaptability across multiple fingers in physical interaction tasks. Therefore, as the next step, this pilot *in vivo* chicken study aimed to evaluate how an in-situ surgically-constructed differential mechanism elicits and reacts to the healing process following surgery.

Materials and Methods: The implant was made of ultra-high-molecular-weight polyethylene and autoclaved before implantation (Figure 1d). Thirty Cornish Cross chickens were randomly assigned to one of three treatment groups: implant-based (Group 1; n=12), sham (Group 2; n=10), and control (Group 0; n=7). During surgery, the Extensor Digitorum Longus (EDL) tendon was exposed where the bifurcation occurs. Group 1 had the implant sutured to the EDL tendon approximately 10mm distal of the bifurcation (Figure 1e). The skin was re-apposed and sutured with non-absorbable material. Group 2 underwent the same surgical procedure as described for Group 1 except the implant was not inserted. Instead, the tendons were sutured with absorbable material. Group 0 did not undergo any surgical procedures. The implant remained in the chickens of Group 1 for approximately 5 to 10 weeks total. Walking ability was periodically assessed on a gait scoring scale from 0 to 5 where 0 denoted normal walking and 5

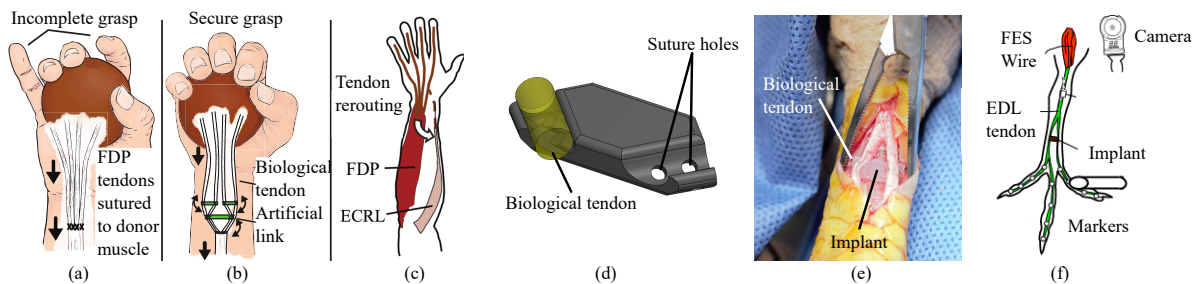
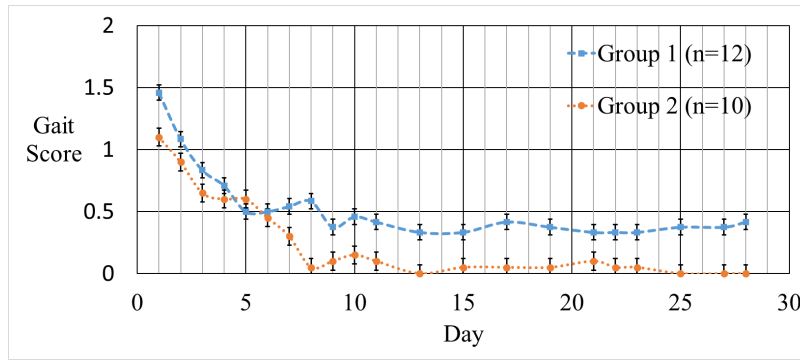


Figure 1: (a) Schematic representing the conventional suture-based tendon-transfer surgery, where the movements of the muscle and tendons are coupled and the fingers are prevented from adapting to the object's shape. (b) Schematic representing the proposed procedure implementing an implantable passive mechanism with attachable artificial links. (c) Schematic representing the hand anatomy and illustrating the re-routing that occurs in the tendon-transfer surgery for high-median ulnar nerve palsy. (d) 3D rendition of the implant illustrating where the biological tendon is positioned. (e) Schematic representing the experimental setup to evaluate toe functionality with motion capture cameras and applying functional electrical stimulation.



Gait score	Degree of impairment
0	None
1	Detectable, but unidentifiable abnormality
2	Identifiable abnormality; little impact on overall function
3	Identifiable abnormality which impairs function
4	Severe impairment of function, but still capable of walking
5	Complete lameness

Figure 2: Mean gait score of Group 1 and 2 per day for 28 days postoperative (left). Walking ability was periodically assessed on a gait scoring scale from 0 to 5 (right) [4].

denoted complete lameness (Figure 2). Furthermore, toe functionality was measured only once per chicken at different time points (5, 6, and 8 weeks) postoperative via functional electrical stimulation (FES) and motion tracking. Each chicken was anesthetized and fine-wire electrodes were subcutaneously inserted into the EDL muscle for FES generated by a Dynatronics® Digital Portable EMS Unit. OptiTrack® motion capture cameras recorded movement of the markers placed on each joint (6) of the lateral toe (Figure 1f). The FES parameters were: 20Hz, 3s ON/6s OFF cycle, and 2s ramp time. After FES testing, each chicken was euthanized and a 3-inch section of tissue, where the implant was or would have been, was harvested from both legs for histopathological examination. Histology data will be reported in a later publication. Total angular movement ($\Sigma\theta$) of toe extension was measured as the sum of each angle at 3 specific joints of the lateral toe (Figure 4).

Results: Observations of scar tissue formation revealed greater tissue build-up in Group 1 than in Group 2 (Figure 3). However, drainage ceased in both groups within 2 weeks postoperative. Subjective gait scores of Group 1 and Group 2 decreased by 1.5 within 8 days postoperative. However, mean gait score remained higher in Group 1 than in Group 2 (Figure 2). One chicken in Group 1 showed a change in total angular movement ($\Delta\theta$) of approximately 7° in the lateral toe when given FES (Figure 5). Toe movement in the other chickens could not be tracked properly due to intense vibration of the toe or lack of extension response when stimulated.

Discussion/Conclusion: These pilot results are encouraging; all chickens healed completely within 2 weeks postoperative as expected. The implant induced greater scar tissue formation

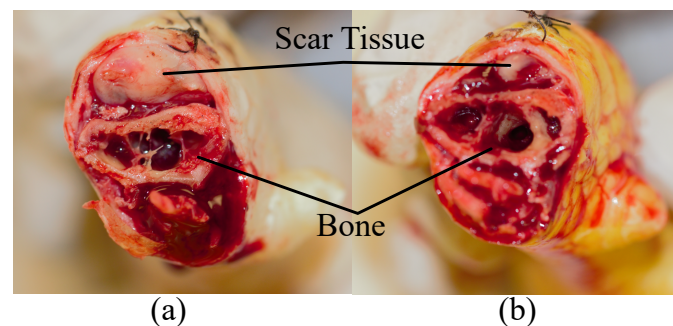


Figure 3: Cross-sectional view just proximal of the surgical site for both Group 1 and Group 2. Overall, Group 1 chickens (a) developed more scar tissue than Group 2 chickens (b).

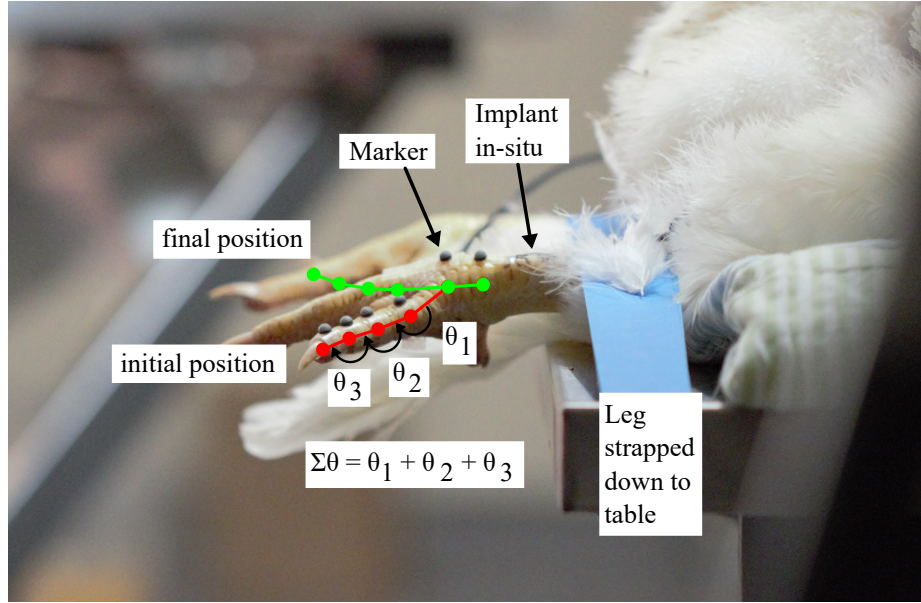


Figure 4: Sedated implanted chicken laying on its dorsal side with legs strapped down to the table. Total angular movement ($\Sigma\theta$) of toe extension was measured as the sum of each angle at 3 joints in the lateral toe ($\Sigma\theta = \theta_1 + \theta_2 + \theta_3$). Each dot in the rigid body models represent each joint in the lateral toe in which a marker corresponded for motion capture tracking. Red model represents the lateral toe at the initial position ($\Sigma\theta_i$) when no FES is applied. Green model represents the lateral toe extending ($\Sigma\theta_f$; final position) during FES.

but movement was only partially hindered as shown by one chicken. However, for most of the other implanted chickens, it can be inferred that scar tissue immobilized the implant attached to the tendons and hindered movement distal of the implant. Additionally, movement could not be tracked properly due to excessive vibration of the toe during FES. Adjustments in FES parameters will be made to reduce rippling in unfused tetanus. Furthermore, to reduce scar tissue formation in the upcoming main study, the following modifications will be explored: re-designing the implant with a smoother profile, applying a non-fouling coating [2], and increasing postoperative physical therapy.

Acknowledgment: Funded by OSU Venture Development Fund and NSF CBET 1554739. We thank Maureen Larson and the OSU LARC staff.

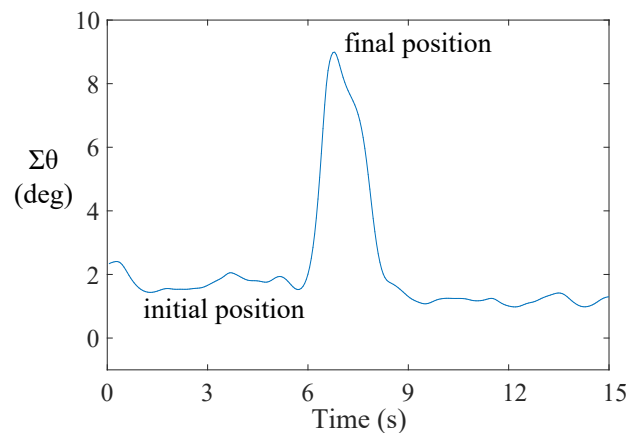


Figure 5: Total angular movement ($\Sigma\theta$) in the lateral toe of an implanted chicken during a stimulation cycle. FES was applied for 3 seconds where the final position was reached and turned off for 6 seconds in which the toe returned to the initial position. Change in total angular movement ($\Delta\theta$) was determined as the difference between the final and initial position ($\Delta\theta = \Sigma\theta_f - \Sigma\theta_i$).

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Histopathological Analysis of Healing Responses to a Novel Tendon Transfer Surgery in a Chicken Model

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Introduction: High median-ulnar nerve palsy is a neuromuscular condition where the median and ulnar nerves in the forearm are damaged. As a result, the Flexor Digitorum Profundus (FDP), Flexor Digitorum Superficialis (FDS), and the intrinsic hand muscles are dysfunctional leading to sensory loss and weakness in the index, middle, ring, and little fingers [1][2][3]. Patients with this condition have impaired flexion function in their four fingers, which affects the performance of physical interaction tasks such as grasping a doorknob. The current surgical procedure for restoring finger flexion is a tendon transfer surgery that detaches the four FDP tendons and sutures them directly to the single Extensor Carpi Radialis Long (ECRL) muscle innervated by the radial nerve [4][5]. While this procedure restores finger flexion, it couples the movements of all four fingers and prevents them from individually adapting to an object's shape during grasping tasks. To address this limitation, we are developing a tendon-transfer surgical procedure that incorporates a passive artificial strut-shaped implant in the tendon network to create a differential mechanism between the ECRL muscle and the four FDP tendons. Our previous studies using human and chicken cadavers have shown that this implant-based surgery significantly improves adaptability of the fingers in physical interaction tasks [6][7][8]. As the next step, our group conducted an in vivo pilot study on a chicken model, using histopathology to evaluate the postoperative healing responses to this novel surgery.

Methods: The implant was made of ultra-high-molecular-weight polyethylene and autoclaved. Twenty-nine Cornish Cross chickens were randomly assigned to one of three treatment groups: control (n=7), implant (n=12), and sham (n=10). During surgery, the Extensor Digitorum Longus (EDL) tendon was exposed with a 1.5 cm incision on the dorsal side of the leg at approximately the same level as the spur. The incision was made in between scales as much as possible, but some scales had to be transected. The EDL tendon was dissected from the surrounding connective tissue at the bifurcation. The implant was placed under and sutured to the EDL tendon branches approximately 10 mm distal to the bifurcation with simple interrupted stitches using 5-0 Prolene (see Fig. 1). The skin was sutured closed with an apposing cruciate pattern using 4-0 Nylon. The sham group underwent the same surgical procedure without implant insertion. Instead, each tendon branch was simply sutured with 5-0 Prolene. The control group did not undergo any surgical procedures. Chickens were euthanized approximately 5 to 10 weeks after surgery, and legs were harvested for routine histopathology. Samples were evaluated for epidermal ulceration, superficial and deep inflammation, hygroma/seroma, fibrosis, periosteal reaction, and cortical resorption. Peritendinous fibrosis levels were graded as absent, mild, moderate and severe.

Results: Both the implant and sham groups had moderate to severe circumferential fibrosis around the tendons, often in close association with fluid-filled cavities (seroma/hygroma) between the tendon and surrounding connective tissue. The control group did not have any peritendinous fibrosis (see Figs. 2 and 3). There was a greater frequency of periosteal reaction in the implant group than in the sham and control groups (6/9 verse 3/8 chickens, respectively). The reaction was more pronounced on the dorsal surface of the metatarsus, frequently accompanied with cortical resorption, in proximity of the implant (see Figs. 2 and 3). Although, the combination of periosteal proliferation and cortical resorption can be an indication of infection, no inflammation or bacteria were identified in histopathology, which suggest that this reaction was sterile. The implant and sham groups had hyperkeratosis of the dorsal skin, but with no indication of epidermal inflammation or ulceration. There was no morphologic evidence of osteomyelitis or deep bacterial infection.

Conclusion: Histopathological responses to injury were similar between the implant and sham groups, with similar peritendinous fibrosis. A marginally greater periosteal reaction in the implant group might warrant implant modifications, including a smoother, thinner profile, a non-fouling coating, with a more minimally invasive attachment mechanism. Overall, the pilot study results were promising as there were no manifestations of infection, no abnormal discharges, and the sutures apposing the skin were not compromised. Nevertheless, we are currently addressing the inherent limitations of the descriptive rank scoring methodology and absence of functional evaluation. We also plan to incorporate both force plate gait analysis and range of motion measurements to supplement the histological data.

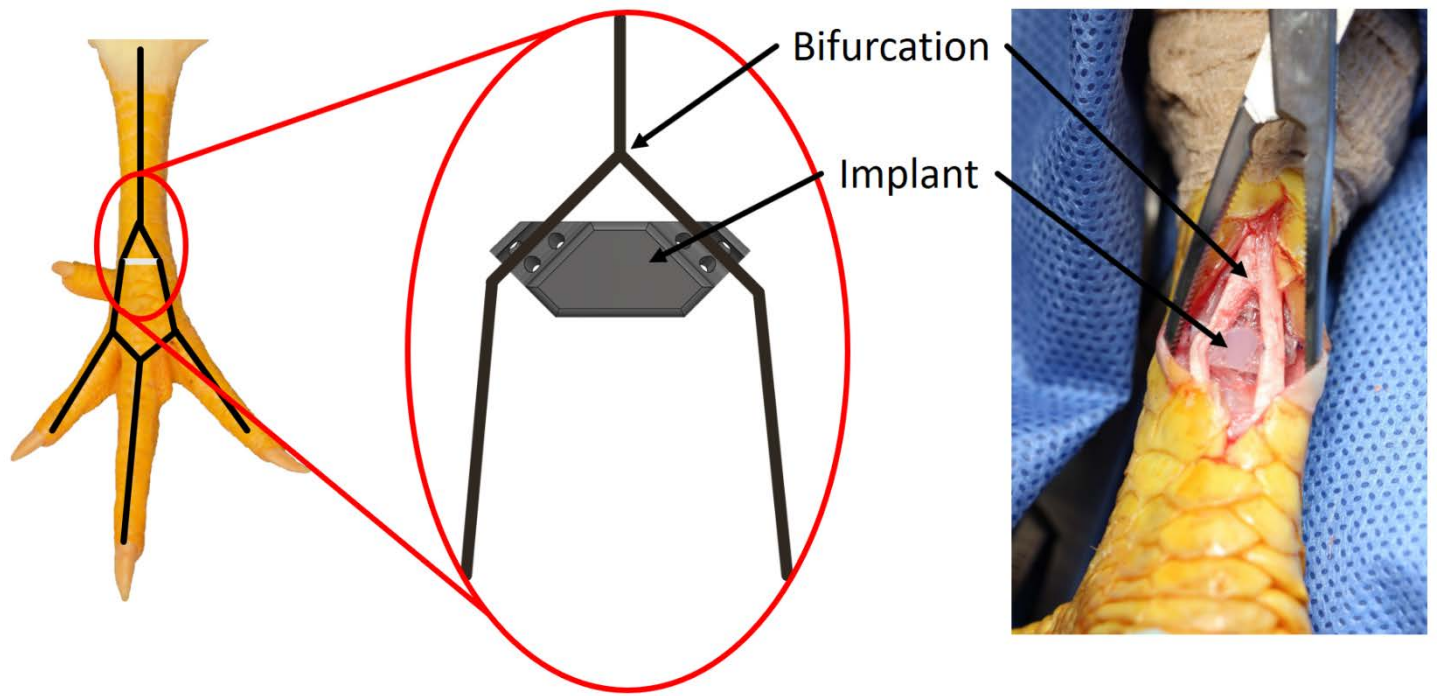


Figure 1: Tendon network outline in the chicken leg with an implant placed just distal to the bifurcation (left and center); implant inserted into the tendon network during surgery (right).

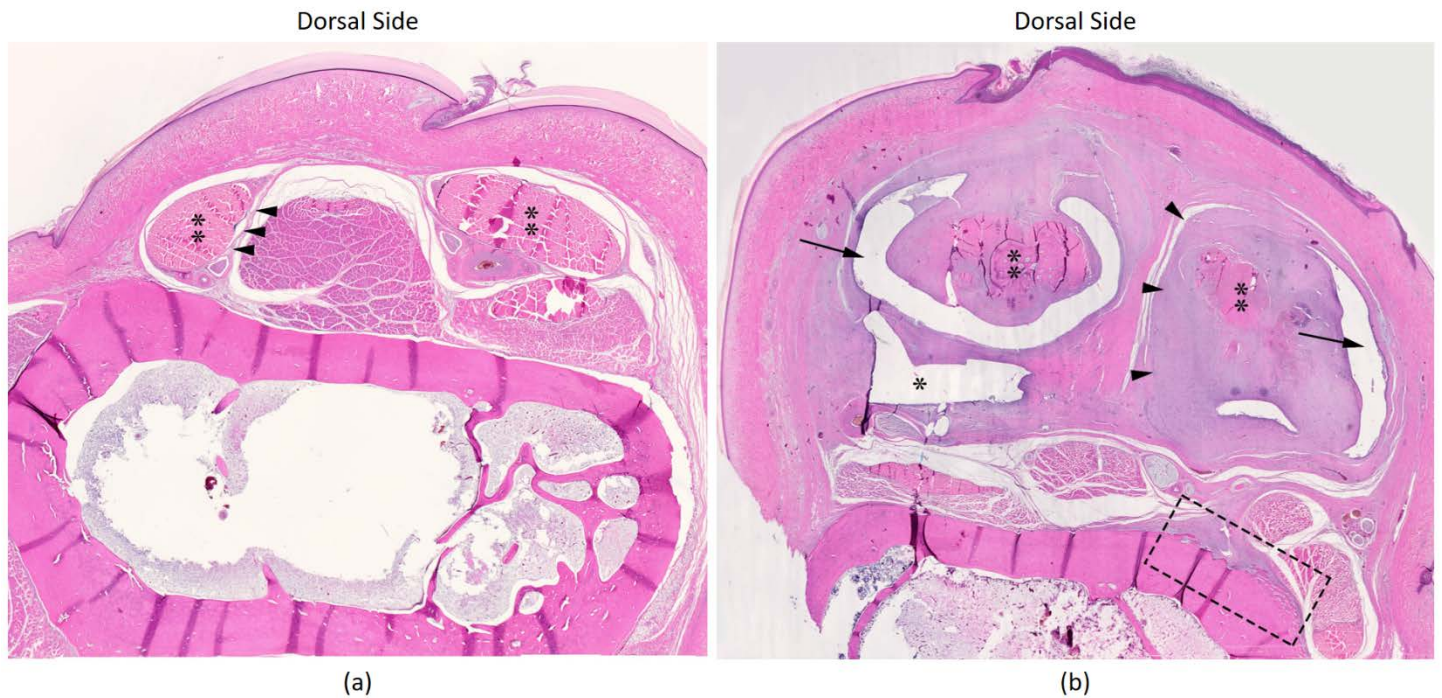


Figure 2: (a) Histology of a control chicken leg stained by Hematoxylin and Eosin, 2x magnification; ** indicates the Extensor Digitorum Longus tendons on dorsal surface of the metatarsus; ► indicates morphologically normal epitenon. (b) Histology of an implanted chicken leg stained by Hematoxylin and Eosin, 2x magnification; * indicates artefactual cavity representing implant location; ** indicates the Extensor Digitorum Longus tendons on the dorsal surface of the metatarsus; ► indicates severe circumferential expansion of the epitenon and surrounding connective tissue by fibrosis; → indicates fluid filled cavity (seroma/hygroma); --- rectangle indicates cortical resorption (scalloped surface in upper half) and periosteal proliferation (lower half).

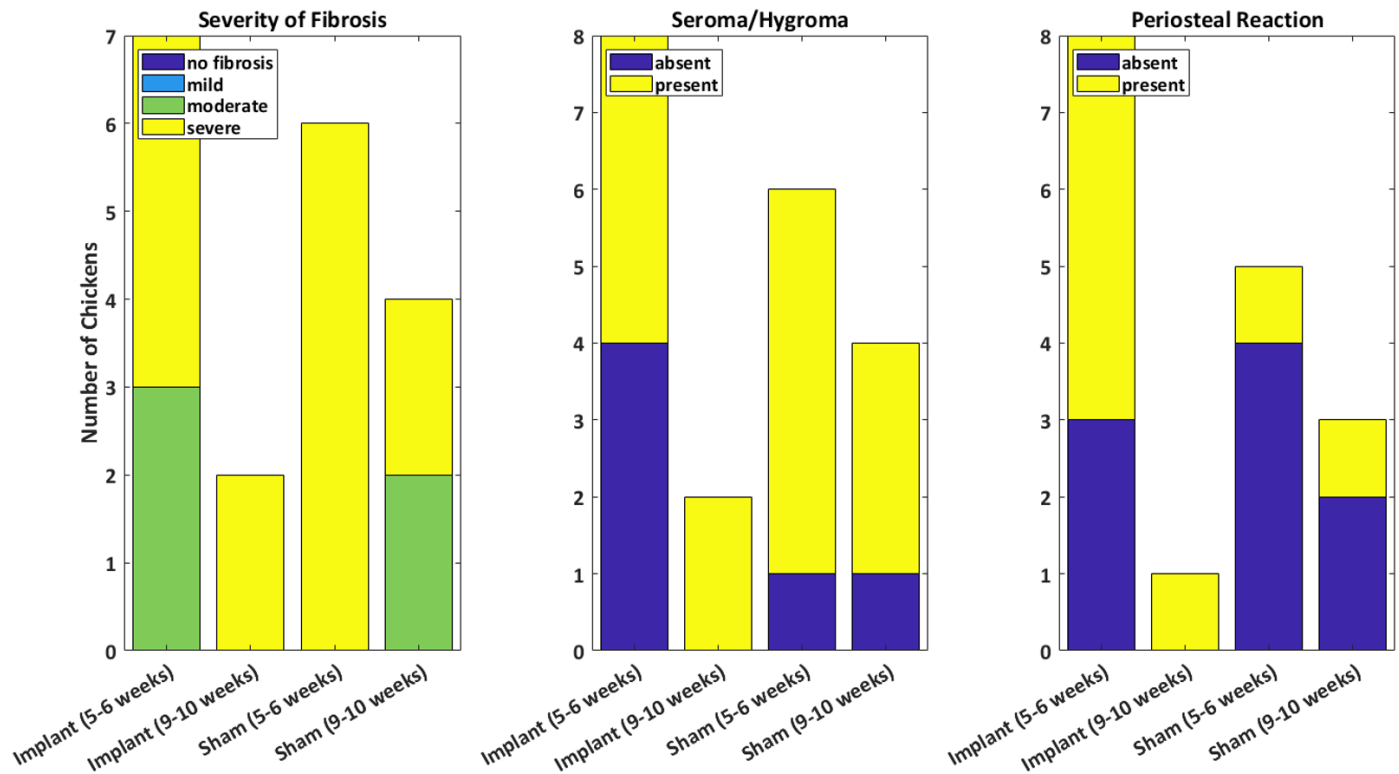


Figure 3: Comparison of fibrosis severity, frequency of hygroma, and frequency of periosteal reactions between the implant and sham groups at 5 to 6 weeks of implantation and at 9 to 10 weeks of implantation. Period of implantation was determined as the time between the surgery and euthanization dates. It is worth noting that these evaluations represent individual chickens, so potential variability can arise within a treatment group. Additionally, it may be concluded that there were more severe cases of fibrosis in the sham group compared to the implant group, but with the inherent limitations of the descriptive rank scoring methodology, the difference between moderate and severe fibrosis may only be marginal. A significance difference in fibrosis severity would be demonstrated if more absent/mild cases of fibrosis were found in one of the groups.

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Histopathological Healing Responses to a Novel Tendon-Transfer Surgery in a Chicken Model

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Background: The conventional tendon-transfer surgery for high-median ulnar nerve palsy involves directly re-routing multiple finger flexor tendons from the Flexor Digitorum Profundus muscle bellies and suturing them to the one Extensor Carpi Radialis Longus muscle belly. While this procedure restores finger flexion, it couples the movements of all four fingers and prevents them from individually adapting to an object's shape during grasping tasks. To address this limitation, our group is developing a new surgical procedure that constructs a differential mechanism in-situ in the forearm using the biological tendons and artificial strut-shaped implants. Our previous studies using human and chicken cadavers have shown that this implant-based surgery significantly improves adaptability of the fingers in physical interaction tasks. As the next step, our group conducted a pilot in vivo chicken study to determine the postoperative healing responses to this novel surgery.

Methods: The implant was made of autoclaved ultra-high-molecular-weight polyethylene. Twenty-nine Cornish Cross chickens were randomly assigned to one of three treatment groups: control (n=7), implant (n=12), and sham (n=10). During surgery, the Extensor Digitorum Longus (EDL) tendon was exposed with a 1.5cm incision on the dorsal side of the leg at approximately the same level as the spur. Then, the EDL tendon was dissected from the surrounding connective tissue at the bifurcation. The implant was placed under and sutured to the EDL tendon branches approximately 10mm distal to the bifurcation with simple interrupted stitches using 5-0 Prolene. The skin was sutured closed with an apposing cruciate pattern using 4-0 Nylon. The sham group underwent the same surgical procedure without implant insertion. Instead, each tendon branch was simply sutured with 5-0 Prolene. The control group did not undergo any surgical procedures. The chickens were euthanized approximately 5 to 10 weeks after surgery and legs were harvested for routine histopathology.

Results: Both the implant and sham groups had moderate to severe fibrosis surrounding the tendons, often in close association with fluid-filled cavities (seroma). Additionally, surface hyperkeratosis was exhibited dorsally in both groups but there was no indication of epidermal inflammation or ulceration. There was a greater frequency of a non-specific (non-compacted and compacted) periosteal reaction in the implant group than in the sham group, where reactions were more pronounced around the implant. Histopathology showed no morphological evidence of bacterial infection.

Conclusion: Responses to surgical injury were similar between the implant and sham groups. However, the marginally greater periosteal reaction in the implant group warrants implant modifications, such as a smoother, thinner profile and potentially a more minimally invasive attachment mechanism.

DESIGN OF A MECHANICALLY ANCHORING IMPLANTABLE MECHANISM FOR TENDON TRANSFER SURGERY

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INTRODUCTION

In previous work, we have shown that it is significantly beneficial to use implantable passive mechanisms to re-engineer the mechanics of force and movement transmission within the body. Specifically, we have shown that we can surgically construct in situ a differential mechanism using biological tendons and a simple strut in a hand tendon-transfer surgery. The differential mechanism enables adaptive finger movement in the fingers even though all four finger tendons are driven by one muscle. Overall, the new implant-based surgery provides significantly better finger flexion than using the current surgery that uses sutures.

A key problem with the current design of this implant is that it needs to be sutured to the tendons (see Figure). This is a problem since the suture is invasive to the tendon, and instigates a fibrotic healing response and long-term scarring. Thus, we seek to re-design the implant so that that it does not have to be sutured to the implant, but will stay secure in the long-term. This paper presents preliminary designs of the implant.

METHODS

The most important requirement of the new implant design is to mechanically anchor it to a tendon without any puncturing which is the most probable cause of fibrosis. To achieve this, the structure of both the 'Zip-tie' and 'Triglidge slide' are adopted to the design (Fig. 2), since both mechanisms provide substantial clamping force to the tendon despite their simple structures. The implant is designed to spiral inward toward axis B as shown in Fig. 2, where the center of the tendon will be located, to provide clamping force with its structural elasticity. The zip-tie by itself is expected to secure the tendon to the implant without having to damage the tendon with sutures. For additional security, as shown in Fig. 3, a thread will be wrapped around the zip-tie and go through the triglide slide to keep the zip tie secured.

RESULTS AND DISCUSSION

As the changes made to the implant involve mechanically securing the tendon, we expect that the implant will work as planned. We also expect that this new attaching mechanism will eliminate the fibrosis that the initial design caused. Moreover, the surgery time is expected to be reduced, since the implant does not require suturing to the tendon.

CONCLUSIONS

In this paper, we presented the new implant design for tendon transfer for median-ulnar nerve palsy. The implant includes the structures of both the 'Zip-tie' and 'Triglidge slide' for mechanically securing the tendon without puncturing it to avoid fibrosis. In the future, this implant

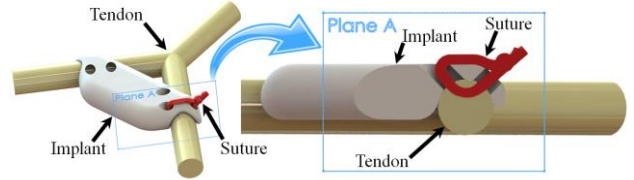


Figure 1: Depiction of the previous implant design and its cross section of plane A.

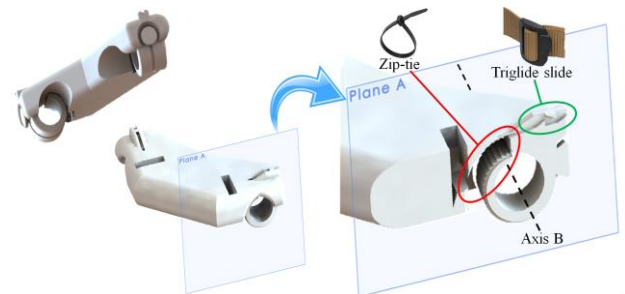


Figure 2: Illustration of the new implant design and its cross section of plane A for orthopedic surgery.

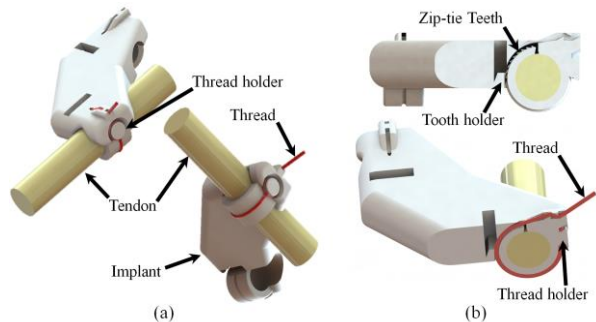


Figure 3: The new implant design (a) anchored on a tendon with both 'Zip-tie' and 'Triglidge slide' mechanism, and (b) cross section of plane A.

design will be validated through a cadaver chicken, live animal and human cadaver study sequentially.

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ACKNOWLEDGEMENTS

This work was supported by NSF CBET 1554739 and DoD CDMRP.

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IMPLANTABLE PASSIVE MECHANISMS FOR DIFFERENTIALLY DISTRIBUTING MOVEMENT ACROSS MULTIPLE TENDONS IN TENDON-TRANSFER SURGERY

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INTRODUCTION

The tendon-transfer surgery for high median-ulnar nerve palsy seeks to restore finger flexion capability by directly suturing the flexor tendons of all four fingers to the wrist extensor muscle (see Figure 1a). While such a surgical procedure is simple, there is an important drawback: the suture couples the flexion of all the fingers. This leads to inconvenient/inappropriate finger movements that compromise tasks such as the grasping of objects. Specifically, the fingers cannot adapt naturally in a staggered manner to the object's shape as the donor muscle contracts. This forces patients to make compensatory wrist and forearm rotations, or use excessive muscle force to close the fingers and establish contact. Overall, the coupled finger movement resulting from the surgery leads to poor grasping capability.

This paper explores the development of implantable miniature passive mechanisms for tendon-transfer surgeries where multiple tendons are sutured to one muscle. These mechanisms, such as pulleys and links inserted between biological tendons, enable "differential action" between the tendons even when driven by one muscle (see Figure 1b). Specifically, the mechanism will distribute the movement provided by the muscle across multiple output tendons while each joint driven by the tendon naturally adapts to external constraints. Importantly, these mechanisms do not require power or control signals, and only mechanically transmit the force and movement from the patient's muscle to the tendons and joints. When applied to the tendon-transfer surgery for high median ulnar nerve palsy, the differential mechanism would enable the fingers to adapt to the object shape naturally even while driven by a single muscle. The mechanism adds an additional passive degree of freedom (rotation of the mechanism itself) to the muscle-tendons-finger biomechanical system, when compared with using the direct suture. This concept is inspired by the use of such mechanisms in the design of "underactuated" robotic hands, where a single motor drives multiple degrees of freedom through these differential mechanisms. This has been shown to improve robotic grasping capability. The challenge in this project is to design these passive mechanisms so that they may be surgically implanted within the human forearm for long-term function.

METHODS

Different embodiments of the passive differential mechanisms are being explored, including the moving pulley and the moving seesaw mechanism. Human cadaver experiments with the pulley embodiment were conducted [1]. In the experiment, the *Flexor Digitorum Profundus* tendons were wrapped around pulley. The pulleys are then driven by a motor in the pulling direction of the *Extensor Carpi Radialis Longus* muscle. The actuation force at

which the fingers establish full contact with a stemmed ball was measured.

RESULTS AND DISCUSSION

Figure 1c compares the actuation force required to close the cadaver fingers with the suture-based procedure or the implant-based procedure [1].

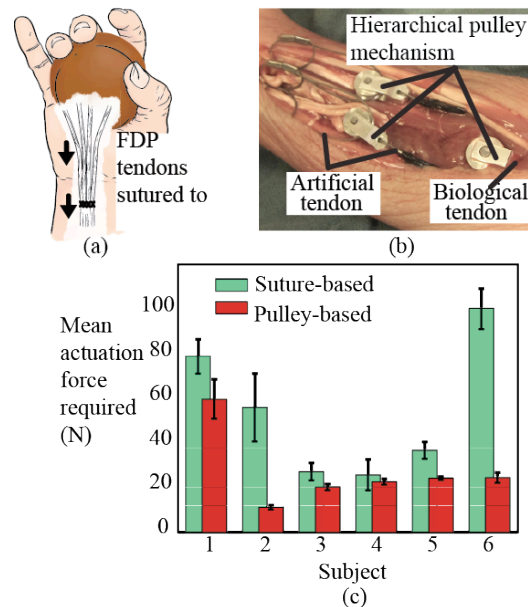


Figure 1: (a) The current suture-based tendon transfer surgery. (b) Human cadaver experiment showing the tendon-transfer surgery using the pulley-based differential mechanism. (c) Force required to close cadaver fingers following the suture-based surgery and the pulley-based surgery [1].

CONCLUSIONS

This paper presents a novel surgical technique for advancing reconstructive tendon-transfer surgeries where multiple tendons are directly sutured to one muscle. By using implanted differential mechanisms between the muscle and the tendons, the human cadaver experiments show that the fingers can adapt better to object at lower actuation forces.

ACKNOWLEDGEMENT

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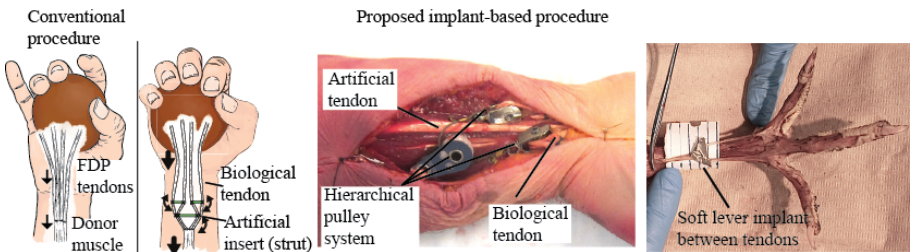
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Study/Product Aim(s)

- Advance orthopedic surgery by developing implantable passive mechanisms for attaching muscles to tendons and bone
- The implantable mechanism will enable customizable force and movement transmission inside the body based on patient’s desired musculoskeletal action
- Expected benefits when compared with current suture-based paradigm: (i) Significantly better joint function; (ii) More surgical choices.

Approach

- Specific Aim 1: To design, fabricate, and validate a miniature biocompatible rod for lateral insertion between two biological tendons.. The validation will be performed through human cadaver and live animal experiments and biomechanical simulation.
- Specific Aim 2: Inhibit fibrosis and reduce interactions between tissue and the implanted mechanism with an immobilized brush of sulfobetaine (SB) polymer.



Preliminary work: Human and animal (chicken) cadaver experiments and biomechanical simulation studies show that the implant-based surgery enables significantly better hand function when compared with using the direct suture in orthopedic surgery

Timeline and Cost

Activities	CY 16	17	18
Specific Aim 1: Design, fabricate implant			
Develop evaluation metrics for implant			
Specific Aim 2: Develop non-fouling layer			
Pilot and full cadaver studies, live animal studies			
Estimated Budget (\$K)	\$500K	\$500K	\$500K

Goals/Milestones

CY16 Goals – Design and fabrication of implantable passive mechanism (lever insert or artificial tendon network) and develop coating

- ❑ Identify the specifications for the implant in terms of strength, movement, fatigue, and biocompatibility requirements. Identify metrics for evaluating implant
- ❑ Conduct pilot cadaver study
- ❑ Develop non-fouling chemical coating

CY17 Goals – Validation of implant in cadavers and pilot study of coating

- ❑ Evaluate the implant in human cadavers (N = 6) in terms of hand function enabled in comparison to hand function enabled by current suture-based procedure.
- ❑ Conduct sensitivity analyses for design using biomechanical simulations
- ❑ Conduct pilot studies of biomaterial coating in mice (N=8)

CY18 Goals – Animal model trials

- ❑ Evaluate implant in live chicken toe-extensor system (N = 18)

Comments/Challenges/Issues/Concerns

- Clinical relevance in human surgery. Will seek advice from orthopedic surgeon.

Budget Expenditure to Date

Projected Expenditure: \$1.5 Million Actual Expenditure: \$325,346